BRONCHOALVEOLAR LAVAGE (BAL) CELLULAR ANALYSES AS A DIAGNOSTIC INTERVENTION FOR PATIENTS WITH SUSPECTED ILD IN CONJUNCTION WITH HRCT IMAGING

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BONAFIDE CERTIFICATE

`This is to certify that the dissertation titled **"Bronchoalveolar Lavage (BAL) Cellular Analyses As A Diagnostic Intervention For Patients With Suspected ILD In Conjunction With HRCT Imaging"** is the Bonafide work done by Dr.C.Ammaiyappan Palaniswamy during his MD (Tuberculosis and Respiratory Diseases) course from May 2013 to April 2015 at the Institute of Thoracic Medicine and Rajiv Gandhi Govt. General Hospital, Madras Medical College, Chennai-3

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DECLARATION

I hereby declare that the dissertation titled **"Bronchoalveolar Lavage (BAL) Cellular Analyses As A Diagnostic Intervention For Patients With Suspected ILD In Conjunction With HRCT Imaging"** submitted for the degree of Doctor of Medicine in MD degree examination branch XVII Tuberculosis and Respiratory Diseases is my original work and the dissertation has not formed the basis for the award of any degree, diploma, associate ship, fellowship or other similar titles. It had not been submitted to any other university or institution for the award of any degree or diploma

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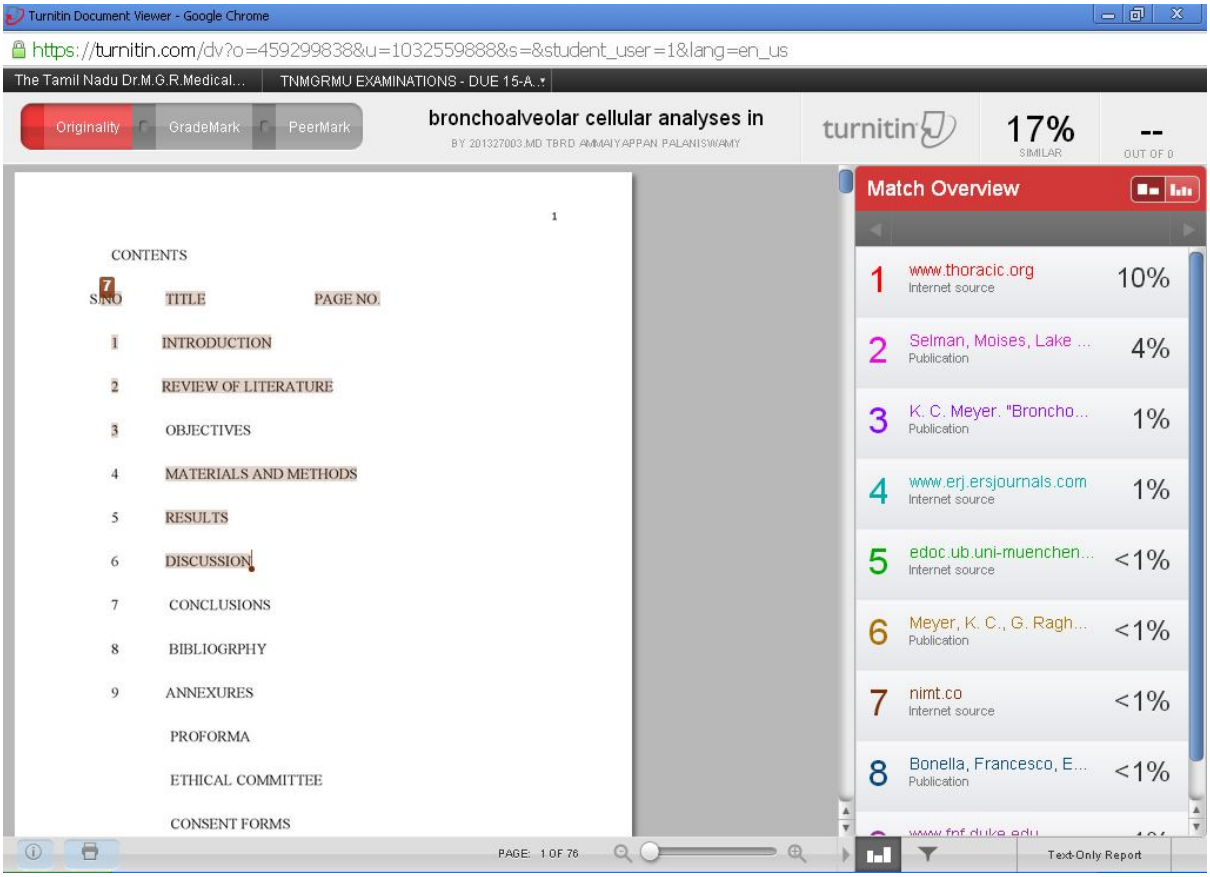
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INTRODUCTION

Diffused infiltrative diseases involving the lung parenchyma with a

differing degree of inflammation and fibrosis that may present acutely or

CONTENTS

Bronchoalveolar lavage (BAL) Cellular Analyses as a Diagnostic Intervention for Patients Suspected with ILD in conjunction with HRCT Imaging

Background

Bronchoalveolar lavage (BAL) has gained acceptance to diagnose interstitial lung disease (ILD). Advent of high resolution computed tomography (HCRT) reduced the clinical utility of BAL. The present work utilized the recommendations of American thoracic society (ATS) to optimize BAL procedure and associated the finding with clinical examination and HRCT to precisely narrow down the cause for ILD.

Method

BAL was performed on ILD suspects at target site chosen based on HRCT. The procedure, transport, processing and analysis of BAL fluid were performed as per ATS guidelines. The clinical data, HRCT findings and BAL report were used to narrow the diagnosis of ILD. Two tailed student T test was used to assess the significance.

Result

We were able to optimize the BAL procedure as per the recommendations of ATS. In the cohort of 50 patients, Idiopathic pulmonary fibrosis (8), hypersensitivity pneumonitis (17), connective tissue disorder (9), sarcoidosis (3), pneumoconiosis (5), ARDS (2), eosinophilic lung disease (2) and lymphangitic carcinomatosa (2), aspiration bronchiolitis (1) and pulmonary histocytosis (1) were diagnosed. Statistically significant variation in differential counts was found in different ILDs. We were able to classify different ILDs based on the criteria described by ATS.

Clinical significance

BAL along with clinical and HRCT findings improved the diagnostic accuracy by incorporating the disease diagnosis, acute or chronic nature of the disease and cause for acute exacerbation, which helped in better management of ILDs.

INTRODUCTION

Bilateral infiltrative diseases involving the lung parenchyma with a varying degree of inflammation and fibrosis, that may present acutely or more commonly as a chronic condition, are as a group named as Interstitial Lung Diseases(ILD). ILDs occur in immunocompetent individuals who do not have a clinical suspicion of infection or neoplasm. ILDs in general are characterised clinically by exertional dyspnoea, radiologically by bilateral pulmonary infiltrates, abnormalities in lung function and gas exchange. Pathological features are excessive collagen deposition along with fibroblastic proliferation, in interstitium, and also in the lumen of the smaller airways.

Chronic ILDs develops over a long duration and comprises of condition with known causes and idiopathic causes. ILDs due to collagen vascular diseases, and work related diseases like pneumoconioses, namely silicosis, asbestosis and coal workers pneumoconiosis and hypersensitivity pneumonitis are diseases with known causes. Interstitial lung diseases without a known cause are a group of disorders named as Idiopathic interstitial pneumonias, and a granulomatous lung disease called Sarcoidosis. Tables 1 and 2 show the clinical and histopathological classification of the ILDs respectively.

Table (1)[1]

Collagen vascular diseases	Scleroderma, polymyositis-dermatomyositis, systemic lupus erythematosus,rheumatoid arthritis, mixed connective tissue disease,Ankylosing spondylitis
Iatrogenic	Antibiotics (notroflurantoin, sulfasalazine), antiarrhythmics (amiodarone, tocainide, propranolol), anti-inflammatories(gold, penicillamine), anticonvulsants(dilantin), chemotherapeutic agents (mitomycin c,bleomycin, busulfan, cyclophosphamide, chlorambucil, methotrexate, azathioprine, BCNU [carmustine], procarbazine), therapeutic radiation, oxygen toxicity, narcotics
Primary (unclassified) diseases	Sarcoidosis, primary pulmonary Langerhans cell, histiocytosis (eosinophilic granuloma), amyloidosis, pulmonary vasculitis, lipoid pneumonia, lymphangitic

	carcinomatosis, bronchoalveolar carcinoma, pulmonary lymphoma, Gaucher's disease, Niemann-Pick disease, Hermansky-Pudlak syndrome, neurofibromatosis, lymphangioleiomyomatosis, tuberous sclerosis, **acute respiratory distress syndrome (ARDS),** AIDS, bone marrow transplantation, postinfectious, eosinophilic pneumonia, alveolar proteinosis, diffuse alveolar hemorrhage syndromes, alveolar microlithiasis, metastatic calcification
Occupational / environment related	Inorganic: silicosis, asbestosis, hard-metal pneumoconiosis, coal worker's pneumoconiosis, berylliosis, talc pneumoconiosis, siderosis (arc welder), stannosis(tin), organic(hypersensitivity pneumonitis), bird breeder's lung, farmer's lung
Idiopathic fibrotic disorders	Acute interstitial pneumonitis(Hamman Rich

	syndrome), idiopathic pulmonary fibrosis/ usual interstitial pneumonia, familial pulmonary fibrosis, respiratory bronchiolitis/ desquamative interstitial pneumonitis, cryptogenic organizing pneumonia, non specific interstitial pneumonia, lymphocytic interstitial pneumonia(Sjogren's syndrome, connective tissue disease, AIDS, Hashimoto's thyroiditis), autoimmune pulmonary fibrosis(inflammatory bowel disease, primary biliary cirrhosis, idiopathic thrombocytopenic purpura, autoimmune hemolytic anemia)

Table[2](2)

Histologic patterns	Clinical Associations
Usual interstitial pneumonia	IPF: connective tissue diseases(uncommon); asbestosis; hypersensitivity pneumonitis; chronic aspiration pneumonia; chronic radiation pneumonitis; Hermansky-Pudlak syndrome; neurofibromatosis
Nonspecific interstitial pneumonia	Idiopathic; connective tissue diseases; drugs; hypersensitivity pneumonitis; diffuse alveolar damage; infections; lymphocytic interstitial pneumonia; AIDS; chronic eosinophilic pneumonia; infections; hemosiderosis; alveolar proteinosis
Diffuse alveolar damage	Acute interstitial pneumonia(Hamman-Rich syndrome); acute respiratory distress syndrome; drugs(cytotoxic agents, heroin, cocaine, paraquat, ethchlorvynol, aspirin); toxic gas

	inhalation; radiation therapy; oxygen toxicity; connective tissue disease; infections(Legionella, Mycoplasma, viral)
Organizing pneumonia	Cryptogenic organizing pneumonia; organizing stage of diffuse alveolar damage; hypersensitivity pneumonitis; eosinophilic pneumonia; Wegener's granulomatosis
Desquamative interstitial pneumonia/ respiratory bronchiolitis	Cigarette smoking; idiopathic; connective tissue diseases; primary pulmonary Langerhans cell histiocytosis; asbestosis; hard-metal pneumoconiosis(cobalt); Gaucher's disease; Niemann-Pick disease; Hermansky-Pudlak syndrome; drugs(nitrofurantoin, amiodarone)
Lymphocytic interstitial pneumonia	Idiopathic; hypogammaglobulinemia; autoimmune disease, including Hashimoto's thyroiditis, lupus erythematosus, primary biliary cirrhosis, Sjogren's syndrome, myasthenia gravis, chronic active

	hepatitis; AIDS; allogeneic bone marrow transplantation.
Eosinophilic pneumonia	Idiopathic acute and chronic; tropical filarial eosinophilia; parasitic infections; allergic bronchopulmonary aspergillosis; allergic granulomatosis of Churg and Strauss; hypereosinophilic syndrome; AIDS.
Alveolar proteinosis	Pulmonary alveolar proteinosis; acute silicosis; aluminium dust; AIDS; myeloproliferative disorder
Diffuse alveolar hemorrhage with capillaritis	Wegener's granulomatosis; microscopic polyangiitis; systemic lupus erythematosus; polymyositis scleroderma; rheumatoid arthritis; mixed connective tissue disease; lung transplantation; drugs(retinoic acid, propylthiouracil, dilantin); Behcet's disease; cryoglobulinemia; Henoch-Schonlein purpura; pauci-immune glomerulonephritis; immune complex glomerulonephritis.

Diffuse alveolar hemorrhage without capillaritis	Idiopathic pulmonary hemosiderosis; systemic lupus erythematosus; Good pasture's syndrome; diffuse alceolar damage; pulmonary veno-occulsive disease; mitral stenosis; lymphangioleiomyomatosis.
Amyloid deposition	Primary amyloidosis; multiple myeloma; lymphocytic interstitial pneumonia.
Granuloma	Sarcoidosis; hypersensitivity pneumonitis; pulmonary Langerhans cell histiocytosis; silicosis; intravenous talcosis; berylliosis; lymphocytic interstitial pneumonia; infections.

Though the causes of ILDs are daunting, the various ILDs have similar characteristics: clinical features, physiologic abnormalities, imaging patterns and histologic patterns. Nevertheless,in many patients, specific diagnosis can be made from clinical history,laboratory tests , HRCT features. Bronchoalveolar lavage(BAL) done by fiberoptic bronchoscope and in some cases transbronchial biopsy of yield a

diagnosis of some ILDs. Surgical Lung Biopsy(SLB) either through a Video assisted thoracoscopic surgery(VATS) or by open thoracotomy maybe required in the remaining cases.

A BRIEF LOOK INTO THE CLINICORADIOLOGICAL, PHYSIOLOGICAL CHARACTERISTICS OF ILDS

The three major hallmarks of ILDs are progressive dyspnoea, characteristic imaging abnormalities, and abnormal lung function tests.[2] But, some patients may have a normal Xray chest at the time of clinical presentation. All the three features need not be present at the time a patient seeks medical attention. A dyspnoeic patient may have a normal spirometry, or a patient with radiologic findings maybe asymptomatic at the time of diagnosis. HRCT of the chest and exercise testing unmasks abnormalities in these patients. BAL can detect abnormalities even when a patient has normal xray or lung function tests, by revealing inflammatory cells,in conditions with high risk of developing ILD like those with CTD, asbestos exposure ,intake of drugs known to cause ILDs or hypersensitivity pneumonitis.

A thorough history is very important. Occupational history should be elaborate as an exposure several years ago can be the cause of the disease in certain conditions. The exposure could have been for a short duration, but of high intensity. Hyperensitivity pneumonitis must be excluded, and it may present as an insidious or as a recurrent acute or sub acute pneumonitis.

DRUG AND TOBACCO HISTORY:

Drug history should include a review of medications used recently as well as in the distant past. Aspiration of gastric contents can lead to ILD. History of tobacco use is important, some ILDs are more predominant in smokers like Pulmonary Langerhans Cell histiocytosis(PLCH), Respiratory bronchiolitis. Smoking also has prognostic value in certain conditions, almost all patients with Goodpastures syndrome have diffuse alveolar hemorrhage,while only one fifth of non smoking patients with Goodpasture's syndrome have alveolar hemorrhage. Also smokers tend not to develop Hypersensitivity pneumonitis(HP) and Sarcoidosis, but in those smokers who develop HP, the disease runs a chronic course. IPF incidence is higher in smokers.

FAMILY HISTORY:

Familial associations are seen in Sarcoidosis, IPF, tuberous sclerosis, Nieman –Picks disease, Gauchers, Hermnsky-pudlak syndromes.

GENDER:

ILDs showing sex predilection are Lymphangioleiomyomatos (LAM) which occurs excusively in women, and CTD associated ILDs are more common in women; whereas Pneumoconioses and occupational ILDs are more likely in men.

SYMPTOMS:

Progressive dyspnoea is the most common symptom. Cough is prominent in Lymphangitic carcinomatosis (LC) and also in Sarcoidosis, cryptogenic organizing pneumonia(COP), Hypersensitivity Pneumonitis, PLCH and Respiratory bronchiolitis. Whezing is associated with CEP. Substernal chest pain can be a symptom in Sarcoidosis. Pleurisy type of pain may occur in drug induced ILDs,CTD-ILDs. Chest pain due to pneumothorax could be a presenting feature of PLCH, tuberous sclerosis, LAM, neurofibromatosis. Hemoptysis is occurs in Diffuse Alveolar Hemorrhage syndromes, and LAM. Hemoptysis in a case of known ILD should raise the possibility of a malignancy complicating ILD.

PHYSICAL FINDINGS:

Bibasilar inspiratory crackles is the most typical auscultatory finding,though they are less likely in granulomatous conditions, followed by digital Clubbing. Clubbing is usually indicative of advanced fibrosis. As the disease progresses, signs of pulmonary hypertension and cor pumonale appear.

PHYSIOLOGIC ALTERATIONS:

Increased elastance, decreased compliance and impaired gas exchange manifest as hypoxia in ABG and a reduced diffusing capacity for carbon monoxide. Assessment of exercise tolerance is the most important physiologic determination in ILD patients and also correlates with disease severity.

HRCT:

With the advent of HRCT the need for invasive diagnostic procedures has reduced. HRCT identifies specific imaging patterns that can strongly support the diagnosis of certain ILDs or can be virtually diagnostic of some.HRCT alone can be diagnostic in the following conditions in the presence of features characteristic to them

- Sarcoidosis

- Idiopathic Pulmonary Fibrosis
- Subacute Hypersensitivity Pneumonitis
- Lymphangitis carcinomatosis
- LCH
- LAM
- Pulmonary alveolar proteinosis (PAP)

HRCT has greatly improved the clinicians ability to shortlist the differential diagnosis, and could be diagnostic in many conditions[1-3]

GALLIUM SCAN:

It is a non invasive test for staging sarcoidosis but is not recommended for IPF, as interpretation is difficult. Its non specific and the scan could be negative in the presence of the disease.

VENTILATION-PERFUSION LUNG SCANNING:

In IPF it shows non segmental inhomogeneities, scattered regions of varying VP match.

ROLE OF MRI :

MRI maybe helpful in differentiation of fibrotic lesion from inflammation.

EXERCISE:

A very important functional parameter in Interstitial lung disease is gas exchange assessment during exercise since it could be normal when the patient is resting.

BRONCHOALVEOLAR LAVAGE:

Bronchoalveolar lavage is done through a fiberoptic bronchoscope which is wedged into a selected bronchopulmonary segment, through which saline is instilled and retrieved. It is done to sample the distal airways. The retrieved sample represents the cellular, immunologic and biochemical mileu.

Methods to analyse the sample and performing the procedure has been setforth by a multicenter publication[3]. BAL could be diagnostic in bronchoalveolar carcinoma; pulmonary lymphoma and lymphangitis carcinomatosa. BAL is therapeutic in pulmonary alveolar proteinosis. BAL could be diagnostic of Langerhans cell histiocytosis if histocytes are in excess of 5%. Populations at risk of ILD, like those with connective tissue disease can be assessed with BAL cellular profile, even in the absence of clinical or radiological evidence of ILD. In such patients BAL reveals increases in inflammatory cell populations.

HISTOLOGICAL DIAGNOSIS:

In the evaluation of an ILD patient, the decision to go for tissue diagnosis is the last step. A thorough history taking leads to a diagnosis in patients with CTD, occupational ILD and drug induced ILDs. But in the case of IIPs, only a suggestive diagnosis may be obtained from clinicoradiological and laboratory findings. And in many a situation, a diagnosis of IPF may only be established by histological findings of usual interstitial pneumonia pattern. When transbronchial biopsy does not yield,the next step is a Surgical lung biopsy. The utility of BAL cell analyses is a subject of difference in opinion as the findings are poor in sensitivity and specificity[4]

The American Thoracic Society(ATS) issued guidelines to increase the yield of BAL in the diagnostic evaluation of ILD and in encourages its use in ILD suspects.

This work utilizes the recommendations put forth by the ATS to optimize the BAL procedure and to associate the findings across different clinical entities of ILD including HRCT.

AIMS AND OBJECTIVES

PRIMARY OBJECTIVE:

To optimize the bronchoalveolar lavage(BAL) procedure as per the recommendations put forth by the American Thoracic Society for the cellular analysis of interstitial lung diseases.

SECONDARY OBJECTIVES:

Optimization of the BAL procedure as recommended by the American Thoracic Society. BAL cellular analyses association with clinical characteristics of different interstitial lung diseases and their radiological findings.

REVIEW OF LITERATURE

The technique of bronchoalveolar lavage(BAL) was first described by Reynolds and Newball in 1974. Though BAL has some limitations, it is additive , if read in the clinical background. R.P.Baughman in his editorial “The uncertainties of bronchoalveolar lavage”has discussed about the retrieval of fluid during the bronchoalveolar lavage procedure and has concluded like this “ as one examines the lavage process closely, one can appreciate the uncertainty a physician may have about the retrieval process. The lavage process itself affects the results. Also, the lung is an active organ, secreting and absorbing protein and cells during the lavage procedure. I doubt that we will ever resolve the uncertainties of dilution that occur during lavage”.

In 2010, Khilnani and Hadda in their editorial titled “Bronchoalveolar lavage: A forgotten tool!” have stated that "a minimally invasive tool for diagnosis which gives a vision into infectious, immunological and inflammatory processes" that occurs at the alveolar level. It is either diagnostic or helpful in revising the differential diagnosis. They have concluded the editorial like this “ although BAL has been used for more than 30 years, quite often this specialised technique is omitted because it is supposed to be a cumbersome procedure with limited diagnostic value. However, with experience it takes few

additional minutes to perform and the information gathered from it adds to the diagnostic value of FOB. Furthermore, therapeutic BAL where large amount of fluid is used to wash lower airway and is used for the treatment of pulmonary alveolar proteinosis. Therefore, it is suggested that every bronchoscopist should be well conversant with this not so commonly used technique."

THE NEED FOR A STANDARD PROCEDURE

There are three populations of cells in the BAL.

1. Cells sampled from alveoli.
2. Cells in alveoli thats not lavaged.
3. Cells from airways that contaminate the lavage sample

Differences in BAL results were due to the differences in the technique of the BAL procedure practised in different parts of the world. Hence, ERS and ATS task force made recommendation for a standard procedure.

SAFETY AND SIDE EFFECTS OF BAL

- The BAL procedure is relatively safe. Side effects if any are usually minor. They include cough and fever after the procedure, transient infiltrates in the chest X-Ray about 24 hours after the procedure, transient deterioration in FVC, FEVI, decreased oxygen tension. When a patient has an underlying disease with respiratory insufficiency supplemental oxygen is to be administered to maintain saturation at 92%. The safety of BAL is well established in adult respiratory distress syndrome(ARDS)[6]. ATS/ERS committee recommends the following regarding the BAL procedure
- routine clinical and laboratory evaluation to diagnose bleeding tendencies
- Site of BAL to be chosen based on HRCT findings, instead of a traditional BAL site
- BAL procedure to be done, with the scope wedged into the selected segment
- the unretrieved volume of instilled saline should not exceed 100ml
- the suction pressure is maintained below 100mm Hg and visual collapse of the airway is avoided.

- if the total retrieved is less than 30% of the instilled saline volume,the differential cell count will be misleading to the clinician
- if the fluid retrieved is less than 5%,the procedure is abandoned to prevent complications
- 20 ml of sample from the entire lavaged fluid is ideal for cell counts analyses

BAL CELLULAR PROFILE IN VARIOUS ILDS AND THEIR CLINICAL APPLICATIONS: ATS CLINICAL PRACTISE GUIDELINES

1. **Idiopathic pulmonary fibrosis (IPF):** IPF is a most frequently diagnosed Idiopathic interstitial pneumonia(IIP), hence,extensively studied. IPF is a distinct condition manifesting in the adult age group, and is characterised by usual interstitial pneumonia(UIP) pattern both pathologically and in high resolution CT scan of the chest. The lavage cellular differential in IPF characterised by predominant macrophages and modest elevation of neutrophils , eosinophils, but lymphocytes levels being normal. But, these features are not specific for ILD. Neutrophils counts range from 5% to 30% in up to 90% of the patients with IPF. The neutrophils percentage may be proportional to the disease extent visualised by

imaging. Eosinophils counts about 5% are seen in up to 60% of the cases. Atypical features are eosinophils >20% or lymphocytes > 15%. , suggest a diagnosis towards ELDs, COP, NSIP, HP, sarcoidosis,superadded infections. While BAL lymphocytosis implies response to steroid therapy, BAL neutrophilia is an independent predictor of mortality. The role of serial BAL to assess prognosis and response to treatment has not been established.

AS A DIAGNOSTIC AID:

- BAL cellular profile as a stand alone test cannot be a confirmatory test
- Typical findings as mentioned above, along with UIP pattern in HRCT chest and supporting clinical criteria may provide a more confident diagnosis
- BAL lymphocytosis >30% is against a diagnosis of IPF.

Prognostic role: not established

2. NONSPECIFIC INTERSTITIAL PNEUMONIA (NSIP)

It is a type of IIP with a better prognosis than IPF. NSIP is a pathological term used in lung biopsy specimens not suggestive of a clear pattern[7]. It is further subdivided based on histopathology as cellular, fibrotic and mixed. Cellular NSIP has the longest survival rate, while fibrotic-mixed is the more common type Clinical presentation maybe of subacute or chronic onset. It is predominant in non smokers and in women.

Lymphocytosis and decreased CD4/CD8 ratio are features of BAL profile in NSIP. Though not very specific, BAL cellular profile along with suggestive clinicoradiological findings can confirm a diagnosis of NSIP. However in fibrotic NSIP, BAL profile is similar to that of IPF/UIP.

AS A DIAGNOSTIC AID:

- Lymphocytosis with reduced CD4/CD8 ratio is seen in cellular NSIP.[8]
- Lymphocytosis is not observed in fibrotic NSIP.
- Diffuse ground glass opacities in HRCT along with BAL lymphocytosis support a diagnosis of cellular NSIP.

PROGNOSTIC VALUE:

Unknown

EOSINOPHILIC LUNG DISEASES(ELD)

ELD refers to a group of different disorders that have a characteristic accumulation of eosinophils as a common feature. With the inclusion of BAL in the diagnosis of ILD, the list of conditions grouped under ELD has expanded substantially,by detecting BAL eosinophilia in the absence of peripheral blood eosinophilia. Since ELD in acute presentation is often mistaken for severe pneumonia of acute origin, diagnosis is not promptly made[9] . Chronic eosinophilic pneumonia(CEP) presents insidiously has a better prognosis.

Conditions that have BAL eosinophilia about 10% and below include chronic granulomatous disorders including tuberculosis and sarcoidosis, fungal diseases, IPF, collagen vascular diseases with lung involvement, pneumocystis carinii pneumonia.

Acute eosinophilic pneumonia clinically presents as an acute febrile illness, which can progress to respiratory failure and is often life threatening. BAL cellular profile shows a marked eosinophilia (>25%) and has a diagnostic value BAL procedure can be done safely in a critically ill patients in whom lung biopsy is not an option. The diagnosis

of AEP is strengthened when the lavage fluid characteristics are similar to that of diffuse alveolar damage[10]. Prompt diagnosis enables early treatment with systemic corticosteroids resulting in rapid and complete recovery Chronic eosinophilic pneumonia(CEP): occurs predominately in females[11]. BAL cellular eosinophilia is diagnostic and responds to corticosteroid therapy. BAL fluid analysis also averts the need for a surgical lung biopsy in these patients

Allergic Bronchopulmonary Aspergillosis(ABPA): is characterised by wheezing, peripheral blood eosinophilia, and lung manifestations of bronchiectasis, a sequela of allergic/immune reaction to aspergillus colonising the airway lumen. ABPA affects previous asthmatics and cystic fibrosis patients. This condition is characterised radiologically by fleeting pulmonary opacities due to eosinophilic aggregation and or mucus plugging. CT findings and clinical features coupled with eosinophilia is characteristic of this condition. BAL fluid shows a high percentage of eosinophilia, which coupled with radiological findings strongly support the diagnosis.

Sarcoidosis is a granulomatous disorder that can involve any organ. It most affects the lungs. Usually occurs in adults. Sarcoidosis is characterised by the presence of hilar adenopathy, lung infiltrations, eye and skin involvement. Due to its varied clinical manifestations and global

prevalence, sarcoidosis can simulate other inflammatory/infectious disorders. Commonly affected organs are the lungs, the lymphatic system, eyes, skin, hepatic, skeletal, cardiovascular and neurological systems.

ATS criteria to diagnose lung sarcoidosis are

i. suggestive clinical features and radiology findings
ii. documenting of non caseating granulomas on biopsy
iii. exclusion of other causes granulomatous inflammation

The sarcoid granulomas have a rim of lymphocytes in their periphery and BAL enables the airspace. Lymphocytes recovery and these are mostly activated T-cells belonging to Th-1-phenotype. Hence, in 1999, ATS/ERS statement included "heightened Th-1 immune response" instead of CD4/CD8 ratio[12] T-cell prominence in granulomatous tissues leads to a reduction in peripheral blood lymphocytes.

BAL has contributed immensely in understanding the immunology and pathogenesis of sarcoidosis. Studies have demonstrated a significant correlation between bal cellular profile and lung biopsy specimens[13-15]. The BAL lymphocytosis correlates with activity of the disease, but a normal lymphocyte percentage can also be seen in the minority of patients. Increased neutrophils are seen in advanced sarcoidosis. Other BAL parameters in sarcoidosis include

neutrophils and eosinophils and a lack of foamy alveolar macrophages.

The diagnostic value of CD4/CD8 ratio has been debated as it shows a high variability in sarcoidosis[14,15], and in a significant proportion of patients this ratio might be decreased. Though CD4/CD8 ratio might be low in sensitivity, it has a specificity of 95% [(16-18)].

The diagnostic value of BAL lymphocytosis is strengthened if CD4/CD8 ratio is also higher [19]

ATS committee concludes that BAL fluid shows an increased lymphocytes but BAL lymphocytosis is not always present. A high CD4/CD8 ratio strongly supports the diagnosis.

A high CD4/CD8 ratio along with BAL lymphocytosis, coupled with clinical and radiological findings suggestive of sarcoidosis strongly support the diagnosis. Neither lymphocytosis nor CD4/CD8 has any prognostic value.

Hypersensitivity pneumonitis (HP) constitutes lung diseases characterised by a granulomatous lung disease that involves airways, alveoli and interstitium due to repeated inhalation of organic and chemical antigens, and sensitisation.

HP is typically characterised by alveolitis with lymphocytes accumulation and granulomatous inflammation.

By clinical presentation, it is classified into acute, subacute and chronic forms. Chronic forms have a variable longterm outcome but often leads an irreversible parenchymal damage. The clinical presentation depends on the nature of the antigen, the amount of exposure, duration of exposure response of Host. HP affects non smokers preferentially[20-23.] The apparent protective effect of smoking is thought to be due to local immune suppressive effects[24,25]. But, smoking does not seem to have a suppressive role once the disease has established [22].

In smokers who develop HP, the disease tends to run a chronic course[26,27]. BAL findings in HP are influenced by the clinical presentation- acute or chronic, smoking habits and the inhaled antigen characteristics.

BAL cellular profile in HP characteristically shows a marked lymphocytosis, often in excess of 50%, whereas lymphocyte percentage under 30% leads to an uncertainty in diagnosis.

The ATS committee has made the following conclusions:

1. With BAL lymphocytosis more than 50% along with clinical and radiological features consist with HP, a confident diagnosis can be made
2. To suspect alternate diagnosis in the absence of BAL lymphocytosis

Prognostic value of BAL in HP is uncertain

CVD/CTD

Understanding of various pattern of diffuse parenchymal lung diseases that affects rheumatological patients has improved considerably in the recent times. Most of this progress from the time of publication of classification of IIP[28.] Diffuse lung disease occur in different patterns in rheumatological diseases. Sub clinical lunseases could be identified in asymptomatic patients diagnosed with a rheumatological diseases when routinely assessed for pulmonary pathology. The histopathological patterns of UIP, LIP, COP, NSIP, DIP and DAD are all seen in rheumatological patients, often coexisting with diseases of the airways such as broncholitis obliterans and

ATS/ ERS task force published ‘clinical guidelines and indications for BAL’ in 1992 in which CTD cases were further divided into CTD with IID and CTD without IID. And the predominant abnormalities reported were an increase neutrophils in RA, Sjogrens and SLE. While SSC had increased neutrophils and eosinophils. And the document concluded that the diagnostic value was limited to differentiating an infection, drug induced disorder or hemorrhage. With more studies focussed on rheumatological disease, clearer messages are emerging.

SSC

Bouros et al[29] studied BAL cellular profile in 73 cases of systemic sclerosis observed elevated neutrophils with elevated eosinophils or elevated lymphocytes. Eosinophils elevation was observed in patient who had NSIP pattern, but not in those with UIP pattern. Lymphocytes elevation was observed in cellular NSIP pattern(on HPE). Furthermore, elevated neutrophils correlated with extensive lesions on HRCT while lymphocytes elevation was present irrespective of any abnormality in HRCT was present or not. Some studies have described that neutrophil excess is a marker of progressive disease[30,31,32] while another studies states that neutrophils excess implies more explosive disease and not a progressive one[33]. Recently two large clinical trials failed to find any useful correlation of BAL cellular profile with either treatment response or progressive of the disease[34,35]

The committee has concluded that the predominant profile in SSc is neutrophilia with or without eosinophilia and lymphocyte is associated with cellular-NSIP. BAL cellular patterns do not determine if treatment is required and do not help to monitor the activity of the disease.

RHEUMATOID ARTHRITIS

In the study by J.G.Garcia et al with a sample size of 24, three groups were observed.

1) Patients with clinical symptoms and radiological evidence of lung disease showing neutrophilia in BAL.

2) Patients with only radiological evidence showing BAL lymphocytosis

3) Third group without clinical and radiological evidence, have a normal BAL cell differential.

These findings interpreted that symptomatic patients with lung lesions had lymphocytosis while diffuse lung disease had BAL neutrophilia. Based on several other studies the committee has concluded that lymphocytosis is a more characteristic feature in RA than in systemic sclerosis.

PRIMARY SJOGREN'S SYNDROME

Based on a few studies in primary sjogren's with lung involvement[36]-salaffi et al and Delavanga et al it has been observed that BAL lymphocytosis is associated with a good outcome while neutrophilia with persistent disease. To sum up conclusions of the ATS committee on clinical applications of BAL profile in all CTD/CVD- related ILDs:

- Adequate studies of BAL in CVD is lacking
- There is a paucity of studies correlating lavage findings with lung biopsy/HRCT findings
- Lymphocytosis is a prominent finding in sjogren's and RA.
- Neutrophilic correlates with extent of pulmonary involvement in HRCT.
- The clinical implication of an abnormal BAL cell differential is not known.

Significance of lavaged cells differential in classification, and in managing of ILD in CTD are not known.

OCCUPATIONAL INTERSTITIAL LUNG DISEASE

In a genetically susceptible person, occupational exposures can cause specific ILD's. These exposures may have occurred several years ago Pneumoconiosis- caused by asbestos, silica and coal dust which get accumulated in the distal airways and lung parenchyma, which is met by a tissue reaction. Metal induced lung disorders that could be granulomatous or fibrotic, induced by beryllium, titanium, aluminum, iron, silver, etc.

SILICOSIS:

Crystalline silica exposure occurs in various occupational settings. Silicotic nodule is the histopathological hallmark of this condition and is formed by macrophages laden with dust and fibrosis tissue surrounding a hyalinised connective tissue.

Eventually as disease progresses these nodules coalesce to produce large conglomerates that involve the pulmonary vessels, airways, and finally producing progressive massive fibrosis (PMF) [37-49]

Bronchoalveolar lavage profiles[37-49] in workers exposed to silica as well as workers who had silicosis had an increase in macrophages which is significant in non-smokers. Lymphocytosis and neutrophilia seems to reflect the ongoing inflammatory process and progression to silicosis.

The committee has conclude that

1) Lavage findings in workers with exposure and workers who had silicosis showed an increased macrophages even in non smoking individuals

2) Lymphocytosis and neutrophilia in BAL are associated with progression to disease.

PULMONARY LANGERHANS CELL HISTIOCYTOSIS

It is a rare condition featuring an abnormal proliferation of langerhans cells.

This disease can be localised or involve multiple systems which were called Hand-Schuller-Christian disease, histiocytosis X, and Letterer-Siwe disease based on the various presentations, is now called Langerhan Cell Histiocytosis(LCH) [51]

Pulmonary LCH(PLCH) has a variable clinical presentation. Most of the patients are smokers with non specific chest symptoms. One characteristic manifestation is recurrent pneumothorax. The pulmonary lesions consists nodules that take bronchiolocentric stellate shape. These contain Langerhans cells , eosinophils, plasma cells and lymphocytes. Eosinophils are found in active stages only.

BAL cellular profile is diagnostic in PLCH and obviates surgical lung biopsy[52,53]. Demonstrating langerhans cells in BAL fluid supports the diagnosis of PLCH in the presence of consistent clinical and radiological features[54]. Immunohistochemical studies or Birbeck granules demonstraton are highly specific for PLCH.

By reviewing literature [55-58,59-64] it has been concluded by the committee that LC differential above 5% is highly supportive of PLCH diagnosis. But, low numbers of LC does not exclude PLCH. It has been observed that as disease progresses, LC percentage decreases.

The committee concludes that

- In the presence of clinical suspicion and suggestive HRCT findings, BAL cellular profile can help to confirm the diagnosis.
- In the absence of the diagnostic HRCT findings, elevated CD1 a staining above 5% of cells is adequate for diagnosis
- BAL finding of less than 5 percent CD1 cells do not exclude PLCH, who have clinical and radiological features consistent with a diagnosis of PLCH.

DRUG INDUCED LUNG DISEASE

Drug induced ILD include a wide range of clinical presentations, mode of onset acute or chronic, lung pathologies and imaging patterns[65,66] which include Eosinophilic pneumonia, pulmonary fibrosis, HP, DAD, DAH, acute non cardiogenic pulmonary edema, and drug induced lupus.

Most common patterns are

1) An acute hypersensitivity response characterised by an elevated eosinophils levels in blood or in airspaces.
2) Subacute/Chronic response that may imitate certain forms of IIP and have fibrosis.

Amiodarone related ILD is characterised by foamy macrophages[67,68]. Nitrofurantoin and methotrexate related ILD is characterised by elevated CD4 lymphocytes[69,70]

Drug induced ILD in a patient with CTD/CVD is often difficult to establish as pulmonary toxicity may be superimposed on ILD that is already present. Nonetheless, HRCT often establishes a pattern that are consistent with specific drug exposures like pulmonary hemorrhage, pulmonary edema, fibrosis, ground glass attenuation. BAL eosinophilia or lymphocytosis suggest a favourable response to corticosteroid therapy.

CONCLUSIONS

1. As a diagnostic aid:

2. BAL cell profile along with HRCT characteristics could aid in diagnosing drug related ILD
3. BAL is also useful to rule out pulmonary hemorrhage/ infections.

RADIATION PNEUMONITIS

Radiation fibrosis and radiation pneumonitis(RP) often complicate radiotherapy of malignancies.

Radiation pneumonitis clinically manifests 1-3 months after radiation in about 8% of patients[71,72]. And radiation fibrosis takes about 6-24 months to evolve and maybe observed in patients who did not suffer from radiation pneumonitis[73] early pathological changes of small vessel injury, congestion and hyaline membrane formation may proceed to a chronic phase if the injury was severe, characterised by progressive septal thickening with vascular sclerosis[74]

BAL lymphocytosis has been observed in the contralateral lung of patients who had radiotherapy for breast cancer[75] which suggests the possibility that radiation pneumonitis may be an immune mediated response of the lung tissue to radiation by generating auto antigens.

Since patients undergoing radiotherapy have other possible causes for radiological infiltrates, BAL is often necessary to exclude hemorrhage, extension of malignancy, infections and drug toxicity. BAL cell profile in RP is characterised by elevated inflammatory cells.

ATS Committee conclusions:

- BAL is useful to exclude other causes of radiological infiltrates like hemorrhage/ infections
- BAL lymphocytosis with consistent clinical and radiological findings supports the diagnosis of radiation pneumonitis.

LYMPHANGITIC CARCINOMATOSIS

BAL cellular analysis usually yield the diagnosis surgical biopsy often unnecessary pneumonitis.

CHRONIC ASPIRATION PNEUMONITIS

Lipid laden alveolar macrophages staining with oil-red O and a semiquantitative scoring method was described by some investigators to diagnose chronic recurrent aspiration.

Identifying pepsin like activity might prove more useful in diagnosing gastric secretions aspiration.

ACUTE ONSET ILD

- Marked elevation of eosinophils in BAL is diagnostic of acute EP.
- BAL helps to diagnose infections and alveolar hemorrhage
- marked elevation of lymphocytes in the background of consistent clinical settings suggests hypersensitivity pneumonitis or drug toxicity.

HRCT IN THE DIAGNOSIS OF ILD

HRCT of the chest has a high sensitivity of 94% for ILD whereas sensitivity of x-ray film is about 80%. HRCT can demonstrate early disease when the x-ray is apparently normal. But, HRCT does not always detect early disease demonstrated by histopathological examination.

A study conducted by Vancouver group in 1989 was the first in establishing a role for CT in diagnosing ILD. They observed that x-ray chest as the first choice correctly diagnosed 77% while CT chest as the first choice diagnosed 93%. Grevier et al reported that by combining clinical, radiographic and HRCT findings the right diagnosis can be done in two thirds of patients. Certain diseases have very characteristic HRCT features obviating a need for biopsy

ILDs which may exhibit very typical HRCT features are:

- IPF
- Sarcoidosis
- Subacute HP
- LC
- PLCH
- LAM
- Alveolar proteinosis.

HRCT PATTERNS AND PROGNOSTIC SIGNIFICANCE:

The ability of HRCT patterns in prediction of treatment response and outcome, etc has been extensively studied.

The ground glass opacity pattern is predictive of a better response to treatment and longer survival than in patients with reticular pattern- in HRCT.

Though at presence evidence is lacking to support HRCT routinely in monitoring the ILD patients, HRCT proves useful in explaining a sudden or unexpected clinical deterioration. HRCT is definitely superior to x-ray chest in diagnosing ILD and also in deciding upon an optimal site for biopsy when required.

BAL/TBLB:In most of the ILDs, correct diagnosis can be made from putting together, clinical, laboratory and HRCT informations.

When HRCT features are typical of IPF,in addition to typical clinical features, surgical lung biopsy will not be necessary. BAL and/or TBLB could increase the diagnostic confidence in certain conditions like malignancy, infection, eosinophilia, HP-subacute, COP, sarcoidosis, rarer conditions like PLCH and PAP.

The decision to perform BAL is informed by patient fitness, differential diagnosis, a supportive laboratory to do BAL cell differential count.

BTS guidelines for TBLB in patients with ILD

- TBLB when needed is to be performed prior to initiating specific therapy.
- Bronchoalveolar lavage is to be considered in rare ILDs, suspected malignancy and infections.
- With clinicoradiological features characteristic of IPF, BAL is necessary as a diagnostic intervention.
- In the absence of typical clinical and radiological features, BAL cellular profile allows a confident diagnosis in sarcoidosis and hypersensitivity pneumonitis.
- In the instance of diagnostic uncertainity where BAL is considered the important diagnostic tool, its preferably done in a center

specialised for the procedures and specialised in analysing the samples

- BAL is to be done in all patients planned for TBLB
- TBLB is the first line procedure in diseases with bronchocentric involvement 4-6 specimens must be taken.
- TBLB is not reliable in rare lung disorders

ILD AND THE UTILITY OF SURGICAL LUNG BIOPSY(SLB): BTS GUIDELINES

SLB is the definitive note of establishing the diagnosis of IPF. SLB excludes infections and malignant processes which may occasionally mimic a chronic ILD. SLB can differentiate CHP from IPF, where CHP is a treatable disease. Disease activity can also be assessed by SLB. HPE diagnostic of IPF has a sensitivity above 60% and specificity almost 97%. Clinical radiological feature can diagnose IPF with a sensitivity and specificity of 48% and 89%.

Studies that contain “changes in therapy” as a reported outcome, SLB contributed more. Hence SLB is ideally done in prior to immunomodulation therapy.

There are two approaches to obtain SLB. One is the traditional limit thoracotomy(OLB) and the other is through a video-assisted thoracoscopic approach(VATS). VATS is being increasingly used now a days. Both these procedures are performed under general anesthesia. Randomized controlled trials that compared open lung biopsy and VATS biopsy reported no significant differences in the time taken for the procedure, complications and diagnostic yield except for a reduced length of stay in hospital in the VATS group.

SLB specimens ideally should be 4cm diameter with a depth of 3-5cm from the pleural space. It should be promptly sent to the pathology laboratory, where it is inflated with formalin. Apart from HPE, PCR, in situ hybridization and immune histochemical techniques maybe applied to make most use of the biopsy specimen.

To summarise the recommendations for SLB in interstitial lung diseases.

- SLB is to be done prior to initiating specific treatments.
- SLB also provides a definitive diagnosis in IPF and other ILDs.
- IPF can be diagnosed with confidence in the presence of typical clinicoradiological picture.
- ILDs require multiple biopsy specimen from multiple lobes.
- Multiple biopsy from differents lobes are easier to do with VATS
- It has lesser early post operative pain compared to OLB.
- Biopsy sites should be chosen based on HRCT findings.

MATERIALS AND METHODS:

Proforma was designed and Institutional ethical committee clearance was obtained.

The nature of the procedure and the purpose of the study was explained in detail to all the patients who were enrolled in this study and informed consent was obtained from all of them. Data was collected as mentioned in the proforma.

SUBJECT SELECTION

Fifty consecutive ILD patients were recruited based on clinical and radiological evaluation after institutional ethics committee approval.

INCLUSION CRITERIA

- ILD patients diagnosed based on clinical and HRCT findings.
- Acute and chronic ILDs in immunocompetent patients
- ILD patients tolerable to the procedure
- Patients above the age of 18 years.
-

EXCLUSION CRITERIA

- ILD patients with bleeding disorders
- ILD patients with cardiorespiratory instability
- Pregnant women
- Pediatric patients

SCREENING PROCEDURES

Patients who were recruited were admitted in our hospital and were subjected to routine blood investigations including HIV testing, HRCT chest, cardiac and rheumatological evaluations.

After obtaining cardiac fitness for the BAL procedure, patients whose respiratory status was adequate, were subjected to the BAL procedure.

BAL PROCEDURE:

- BAL was done using a flexible bronchoscope wedged into the chosen bronchopulmonary segment
- The bronchopulmonary segment to be lavaged was selected based HRCT findings-areas with GGOs, profuse nodular lesions or thin reticulations were- optimal targets
- Patients in whom the lavage site was other than the right middle lobe, positioning of the patient was adjusted retrieval.
- The total volume of saline instilled was about 240ml, in aliquots of 60ml. In all the patients, the retrieval volume was more than 100ml. Four sequentially instilled aliquots were withdrawn [6]
- The first retrieval sample was sent for microbiological analysis
- The samples were collected into a mucus extractor whose capacity was 25ml. about 4 to 5 such containers of sample was collected

from each patient and transported to the cytology laboratory in an ice box which maintains a temperature of 4^{o}c.

- Arrangements were made to analyse the sample for total cell counts, differential cell counts within one hour of the BAL procedure.
- Throughout the BAL procedure, oxygen saturation of the patient was monitored and maintained above 92%
- The suction pressure used during the procedure was under 100mmHg, and was further adjusted to avoid visible airway collapse.
- Before the sample was sent to the laboratory, gross appearance of the fluid was noted.
- The BAL samples were pooled together in the laboratory and about 20ml of the pooled sample was used for the cellular analysis.

TABLE 3:

SUMMARY OF BAL CELLULAR PATTERNS IN NORMAL/HEALTHY ADULT NONSMOKERS AND IN PATIENTS WITH COMMON INTERSTITIAL LUNG DISEASES (CONSISTENT PATTERNS AND CLINICAL UTILITY)

I. Normal Adults (Nonsmokers)	**BAL Differential Cell Counts**
Alveolar macrophages	85%
Lymphocytes (CD41/CD81 ¼ 0.9–2.5)	10–15%
Neutrophils	<3%
Eosinophils	<1%
Squamous epithelial*/ciliated columnar epithelial cells†	<5%

LYMPHOCYTIC CELLULAR PATTERN **>15% LYMPHOCYTES**	**EOSINOPHILIC CELLULAR PATTERN** **>1% EOSINOPHILS**	**NEUTROPHILIC CELLULAR PATTERN** >3**% NEUTROPHILS**
Sarcoidosis	Eosinophilic pneumonias	Collagen vascular diseases
Nonspecific interstitial pneumonia (NSIP)	Drug-induced pneumonitis	Idiopathic pulmonary fibrosis
Hypersensitivity pneumonitis	Bone marrow transplant	Aspiration pneumonia
Drug-induced pneumonitis	Asthma, bronchitis	Infection: bacterial, fungal
Collagen vascular diseases	Churg-Strauss syndrome	Bronchitis
Radiation pneumonitis	Allergic bronchopulmonary aspergillosis	Asbestosis
Cryptogenic organizing pneumonia (COP)	Bacterial, fungal, helminthic, Pneumocystis infection	Acute respiratory distress syndrome (ARDS)
Lymphoproliferative disorders	Hodgkin’s disease	Diffuse alveolar damage (DAD)

II. Interstitial lung diseases

a. Disorders associated with increased percentage of specific BAL cell types

b. Abnormal BAL differential cell patterns that suggest specific types of ILD

A lymphocyte differential count >25% suggests granulomatous disease (sarcoidosis, hypersensitivity pneumonitis, or chronic beryllium disease), cellular nonspecific interstitial pneumonia, drug reaction, lymphoid interstitial pneumonia, cryptogenic organizing pneumonia, or lymphoma.

CD4/CD8 is highly specific for sarcoidosis in the absence of an increased proportion of other inflammatory cell types. A lymphocyte differential count >50% suggests hypersensitivity pneumonitis or cellular nonspecific interstitial pneumonia. A neutrophil differential count >50% supports acute lung injury, aspiration pneumonia, or suppurative infection.

c. Other abnormal BAL findings

Infectious organism	Lower respiratory infection
Malignant cells (light microscopy, flow cytometry)	Cancer
Bloody fluid that increases in successive aliquots	Pulmonary hemorrhage 6 diffuse alveolar damage
Milky fluid with positive periodic acid Schiff staining and amorphous debris	Pulmonary alveolar proteinosis
In vitro lymphocyte proliferative response to specific beryllium antigen	Chronic beryllium disease
Definition of abbreviation: BAL bronchoalveolar lavage.	
* The presence of squamous epithelial cells indicates upper airway secretion contamination.	
[y] Epithelial cells >5% suggest suboptimal sample (BAL cellular patterns should be interpreted with caution).	

The above table was from ATS clinical practise guidelines is a reference used in this study and based on this we grouped Cellular patterns from the results obtained. “ The reason for routine cellular analysis whenever BAL is performed in a patient with suspected ILD is that identification or exclusion of the predominantly inflammatory cellular pattern may support a specific type of ILD or help narrow the differential diagnosis when considered in the context of the clinical and radiological findings. The notion that a prominence of specific nucleated inflammatory or immune cells in the BAL correlates with an increased likelihood of certain types of ILD is supported by numerous accuracy studies that are limited by risk of bias. These include pronounced BAL eosinophilia in eosinophilic pneumonia[77,78], drug reactions[79,81], BAL lymphocytes in sarcoidosis[82-85], hypersensitivity pneumonitis[86-88], pneumotoxic drug reactions[89,90] or cellular NSIP[91,92]”.

Follow up procedures

The patients who had undergone the procedure were observed for 48 hours for post procedure bleed, followed up with chest x-rays immediately and 24 hours after the procedure. Those who did not require inpatient treatment were discharged with care.

ASSESSMENTS OF PARAMETERS

TECHNIQUE OF BAL CELL ANALYSIS

The cellular analysis is performed within an hour from the time of procedure. The total cell count was done with a hemocytometer, and the viability of the cells was analysed by Trypan blue exclusion. The differential counting was done by cytocentrifugation after Wright-Giemsa staining and enumeration of at least 400 cells. The presence and relative numbers of erythrocytes and epithelial cells were noted. The presence of squamous epithelial cells suggests that BAL fluid is contaminated with upper airway secretions, and the presence of large numbers of bronchial epithelial cells suggests that the BAL may not have adequately sampled distal airspaces. Excess BAL fluid was stained and cultured for mycobacteria and fungi in the microbiology laboratory, as well as screened for neoplastic cells. These were important additional tests to consider because infections and diffuse neoplasms can masquerade as ILD or coexist with ILD.

INTERPRETATION OF BALL DIFFERENTIAL COUNTS

The ranges of differential cell counts that are considered normal and abnormal derive from several sources. Numerous investigators have published BAL immune cell profiles from cohorts of clinically normal volunteer subjects recruited in single-center studies[92-98] and these reports have been used to define normal and abnormal differential cell counts. In addition, the multi-center BAL Cooperative Study[92] reported the differential cell counts in the BAL of normal subjects (including smokers or ex-smokers) compared with patients with ILD. An increased number of nucleated immune cells and abnormal proportions of immune cell types may suggest or support specific types of ILD in the absence of an infection. A mixed cellular pattern can be observed with any ILD; when mixed cellular patterns are observed, the dominant cell type may be the most consistent with a specific ILD diagnosis. A BAL fluid cell differential count with greater than 15% lymphocytes, greater than 3% neutrophils, greater than 1% eosinophils, or greater than 0.5% mast cells indicates BAL lymphocytosis (i.e., a lymphocytic cellular pattern), BAL neutrophilia (i.e., a neutrophilic cellular pattern), BAL eosinophilia (i.e., an eosinophilic cellular pattern), or BAL mastocytosis, respectively. A lymphocyte differential count greater than or equal to 25% suggests granulomatous lung disease (e.g., sarcoidosis, HP, NSIP, chronic beryllium disease, drug reaction, LIP, COP, or lymphoma), while a

lymphocyte differential count greater than 50% is particularly suggestive of HP or cellular NSIP. An eosinophil differential count greater than or equal to 25% is virtually diagnostic of eosinophilic lung disease in the appropriate clinical setting. A neutrophil differential count greater than or equal to 50% strongly supports acute lung injury, aspiration pneumonia, or suppurative infection. Finally, a mast cell differential count greater than 1% combined with a lymphocyte differential count greater than 50% and a neutrophil count greater than 3% is suggestive of HP. A predominance of macrophages containing smoking-related inclusions with no or minor increases in other cell types is compatible with smoking-related ILD, such as DIP, RBILD, or pulmonary Langerhans cell histiocytosis (PLCH). Additional tests to identify and count Langerhans cells in the appropriate clinical setting may be useful in narrowing the differential diagnosis. A predominance of hemosiderin-laden macrophages is suggestive of chronic or occult alveolar hemorrhage syndromes resulting in pulmonary hemosiderosis or diffuse alveolar damage.

ATS Recommendations "For patients with suspected ILD in whom BAL is performed, the lymphocyte subset analysis NOT be a routine component of BAL cellular analysis. The lymphocyte subset analysis (by cytometry or immunocytochemistry) will not be performed routinely, but rather would be performed if a lymphocytic disease is suspected or the initial BAL cellular findings identify a lymphocytosis. This suggestion is based upon the committee's clinical experience that lymphocyte subset analysis is rarely helpful and potentially misleading in the absence of a clinically suspected lymphocytic disease or a lymphocytosis. Many investigators have characterized lymphocyte subsets on the basis of T helper (CD41) versus T suppressor (CD81) phenotypes, and have found correlations of the CD41/CD81 T lymphocyte ratio with specific disease processes such as sarcoidosis and hypersensitivity pneumonitis[86,87,99,100]. However, subsequent investigations have found that the CD41/CD81 ratio may not be significantly increased in a substantial number of patients with sarcoidosis[101,102] or significantly decreased in a substantial proportion of patients with hypersensitivity pneumonitis[103,104], and can change during the course of the disease process. In addition, the BAL CD41/CD81 T lymphocyte ratio varies with age and may be significantly increased in normal subjects[105]. These issues are discussed extensively in the portion of the online supplement that pertains to specific forms of ILD. However,

in the case of sarcoidosis, the combination of BAL lymphocytosis combined with a considerably increased BAL CD41/CD81 lymphocyte ratio (e.g., > 4) may increase the confidence of a diagnosis of sarcoidosis if other clinical features and imaging are consistent with this diagnosis, and lymphocyte subset determinations may be performed at the discretion of the pulmonologist if such analysis can be reliably performed in the clinical laboratory and is considered to be clinically useful. Finally, there are other tests that can be performed on BAL fluid on a case-by-case basis and may be helpful in specific clinical circumstances. Analysis by a cytopathologist is indicated if there are isolated cells that are suspicious for malignancy. Periodic Acid Schiff staining or Oil Red O staining may be helpful if pulmonary alveolar proteinosis or aspiration is suspected, respectively. Hemosiderin staining may be performed if hemorrhage is suspected and/or the initial BAL raises the suspicion of hemosiderin-laden macrophages".

STATISTICAL ANALYSIS:

Non parametric analysis was performed on the cohort after finding the median values of different cell counts obtained from the fluid analysis. Overall significance of the cell counts between different ILD's was assessed using SPSS version.13(SPSS, chicogo,IL) and $P< 0.05$ was considered significant.

STUDY DESIGN:

Prospective continuous study

RESULTS:

Fifty consecutive ILD patients were recruited for the study after obtaining informed consent. Clinically suspected ILD patients were subjected to HRCT and based on HRCT findings, BAL was performed after selecting the site for fliud collection in the lungs, except for two patients with ARDS. The procedure, transport, processing and analysis of BAL fluid were performed as per ATS guidelines. The patients were segregated based on the ATS classification given in table 3.

TABLE 4

DD1 LYMPHOCYTIC CELLULAR PATTERN	DD3 EOSINOPHILIC CELLULAR PATTERN	DD2 NEUTROPHILIC CELLULAR PATTERN
>15% lymphocytes	>1% eosinophils	>3% neutrophils
sarcoidosis	Eosinophilic pneumonias	Collagen vascular diseases
Nonspecific interstitial pneumonia(NSIP)	Drug-induced pneumonitis	Idiopathic pulmonary fibrosis
Hypersensitivity pneumonitis	Bone marrow transplant	Aspiration pneumonia
Drug-induced pneumonitis	Asthma, bronchitis	Infection: bacterial, fungal
Collagen vascular diseases	Churg-strauss syndrome	Bronchitis
Radiation pneumonitis	Allergic bronchopulmonary aspergillosis	Asbestosis
Cryptogenic organizing pneumonia(COP)	Bacterial, fungal, helminthic, pneumocystis infection	Acute respiratory distress syndrome(ARDS)
Lymphoproliferative disorders	Hodgkin’s disease	Diffuse alveolar damage(DAD)

DD4(lymphocyte differential count>=25%)	DD5(lymphocyte differential count>50%)	DD6(neutrophil differential count>50%)	DD7(eosinophil differential count>25%)	DD8(cell differential count >1%mast cells
Suggests granulomatous disease(sarcoidosis, Hypersensitivity pneumonitis or chronic beryllium disease), cellular nonspecific interstitial pneumonia,drug reaction,lymphoid interstitial pneumonia, cryptogenic organizing pneumonia or lymphoma. CD4+/CD8+>4 is highly specific for sarcoidosis in the absence of an increased proportion of other inflammatory cell types.	Suggests hypersensitivity pneumonitis or cellular nonspecific interstitial pneumonia.	Supports acute lung injury, aspiration pneumonia or suppurative infection.	Virtually diagnostic of acute or chronic eosinophilic pneumonia.	>50% lymphocytes and > 3% neutrophils is suggestive of acute hypersensitivity pneumonitis.
OTHER ABNORMAL BAL FINDINGS				

Infectious organism	**Lower respiratory infection**
Malignant cells(light microscopy, flow cytometry)	Cancer
Bloody fluid that increases in successive aliquots	Pulmonary hemorrhage, diffuse alveolar damage
Milky fluid with positive periodic acid Schiff staining and amorphous debris	Pulmonary alveolar proteinosis
In vitro lymphocyte proliferative response to specific beryllium antigen	Chronic beryllium disease

The segregation of the cohort as per the clinical diagnosis is as follows: idiopathic pulmonary fibrosis(IPF-8), hypersentivity pneumonitis(CHP-17), connective tissue disorder(CVD-9), sarcoidosis(SAR-3), pneumoconiosis(SIL-5), ARDS(2), eosinophilic lung disease(ABPA-2) and lymphangitic carcinomatosa(LC-2), aspiration bronchiolitis(AB1) and pulmonary histocytosis(PLCH) The demographic data and the finding are listed in table 5.

S.NO	ID#	AGE/SEX	S	A	EXP	D.O.I	PFT	RHE	BAL1	BAL2	HRCT DD	CLI+BAL	CLI+BAL+HRCT+OTHERS
1	IPF1	49/M	–	–	O.D	2yrs	Res	–	DD1,DD2	DD6,DD4	UIP-DD IPF,NSIP,CHP	IPF,NSIP,ALI,S.A.I	IPF-AE+SAI
2	IPF2	56/M	+	–	–	2yrs	Res	–	DD1,DD2	DD4	UIP-DD	IPF	IPF
3	IPF3	52/M	+	–	–	3`yrs	Res	–	DD1,DD2	DD3,DD4	UIP-DD	IPF,BA,ELD,INF	IPF-AE BRONCHITIS SAI
4	IPF4	37/M	–	–	–	Yrs	Res	–	DD1,DD2	DD4	UIP-DD	IPF,CHP	IPF
5	IPF5	50/M	+	+	–	3yrs	Res	–	DD1,DD2,DD3	DD4	UIP-DD	INF,IPF,ELD,BA,ABPA	IPF-AE+SAI

6	IPF6	54/M	_	+		1yr	Res	_	DD1,DD 2	_	UIP-DD	IPF	IPF
7	IPF7	64/M	+	+		4yrs	Res	_	UPPER AIRWA Y	COMTA MINATI ON	UIP	IPF	IPF
8	IPF8	49/M	+	_		6months	Res	_	LCH	LCH	?CYSTI C DISEAS E?+IPF(p lain CT)	LCH	LCH
9	IPF9	50/M	_	_	_	4yrs	Res	_	DD1,DD 2	–	IPF FIB-NSIP INF	IPF-AE SA.I	IPF-AE SAI
10	HP1	75/M	_	+	PEST	20yrs	Res	_	DD1,DD 2	DD4	CHP,NSI P,SAR	CHP,INF	CHP,SAI
11	HP2	55/M	+	+	_	10yrs	Res	_	DD1,DD 2,DD3	DD4	SIL,SAR, CHP,NSI P	HP,SAR, BA,INF, NSIP	HP,SAI

12	HP3	61/F	–	–	COTTON	15yrs	Res	–	DD2	DD6	SIL,SAR, CHP,NSIP,B'LIMS	AP,SI,ARDS	CHP,SAI
13	HP4	55/M	–	–	POULTRY	10yrs	Res	–	DD1,DD2	DD4	HP,SAR, NSIP,AIP	IPF,SAR, CHP	CHP,SAI
14	HP5	65/M	+	+		40yrs	Res	–	DD1,DD2	DD4	HP,SAR, SIL,NSIP ,IPF	HP,SAR, NSIP,BRONCHITIS	CHP,SAI
15	HP6	37/M	–	+		18yrs	Res	–	DD1,DD2,	DD4	DD-FIBROSIS,DD-CLN	HP,SAR, NSIP-CEL	HP-Subacute
16	HP7	58/M	–	+		15yrs	Res	–	DD1,DD2	DD4	DD-FIBROSIS	HP,SAR, IPF	HP
17	HP8	25/F	–	–		14yrs	Mxd	–	DD1,DD2	DD5	AHP,DD-GGO,DD-CLN	HP,AHP	Acute HP

18	HP9	58/M	_	_	PEST	40yrs	Res	_	DD1,DD2	DD4	DD-FIBROSIS	IPF,HP,NSIP	CHP
19	HP10	58/F	_	_		15yrs	Res	_	DD1,DD2	DD4	DD-FIBROSIS	HP,IPF,NSIP,SAR,SAI	CHP,SAI
20	HP11	26/M	_	_		20days	Mxd	_	DD1,DD2	DD5	DD-GGO,DD-CLN,AHP	HP,NSIP,SAR	AHP
21	HP12	58/M	_	_	PEST	10yrs	Res	_	DD1,DD2	DD4	DD-FIBROSIS	HP,NSIP,SAR,INF	CHP
22	HP13	73/M	_	+	PEST	20yrs	Res	_	DD1,DD2	DD4	CHP,IPF	CHP,SAR,IPF	CHP
23	HP14	48/M	+	_	_	15yrs	Res	_	DD1,DD2	DD4	CHP,IPF	CHP,SAR,IPF,NSIP	CHP

24	HP15	55/M	_	_	BIOMASS	5yrs	Res	_	DD1,DD2		IPF,CHP	IPF,CVD,SAR,SIL	CHP
25	HP16	60/M	_	+	PEST	6yrs	Res	_	DD1,DD2	DD4	DD-FIBROSIS	HP,NSIP,SAR	CHP
26	HP17	30/M	_	+	WELD	3yrs	Res	_	DD1,DD2	DD4	DD-FIBROSIS	HP,NSIP,SAR	CHP
27	CVD1	45/F	-	-	-	1YR	RES	RA	DD1,DD2	DD5	DD-INTERLOOBAR SEPTAL THICKENING+UIP	CVD,IPF,NSIP,HP	CVD-ILD
28	CVD2	61/F	-	-	-	2YRS	RES	RA	DD1,DD2	DD4	UIP,DD	IPF,CVD,BRONCHITIS	CVD-RA-ILD
29	CVD3	38/M	-	-	-	2YRS	RES	RA	DD1,DD2		DD-GGO	IPF,CVD,CHP,BRONCHITIS	CVD-RA-ILD

30	CVD4	52/F	-	-	-	1YRS	RES	RA	DD1,DD2	DD4	DD-GGO,NSIP	CVD,IPF,BRONCHITIS	CVD-RA-ILD
31	CVD5	64/F	-	-	-	1YRS	RES	RA	DD1,DD2	DD4	DD-GGO	IPF,CVD	CVD-RA-ILD
32	CVD6	44/M	+	+	-	3YRS	RES	RA	DD1,DD2	DD4	DD-GGO	IPF,CVD,INF,BRONCHITIS	CVD-RA-ILD
33	CVD7	22/F	-	-	-	ASYMPTOMATIC	RES	SSc	DD,DD2		IPF/CVD	IPF,CVD,NSIP,	CVD-SSc-ILD
34	CVD8	26/F	-	-	-	ASYMPTOMATIC	RES	SScc	DD2		DD-UIP	IPF,CVD,INF	CVD-SSc-ILD
35	CVD9	48/F	-	-	-	1YR	RES	RA	DD1,DD2		DD-GGO+HONEYCOOMB	IPF,CVD,HP	CVD-RA-ILD

36	SAR1	25/F	-	-	-	NIL RESPIR ATORY	NORMA L	-	DD1,DD 2	DD4	TB,SIL,S AR,LYM PHOMA	TB/SAR	SARCOI DOSIS
37	SA2	62/F	-	-	-	NIL RESPIR ATORY	NORMA L	-	DD1,DD 2	DD4	-DO-	TB/SAR	SARCOI DOSIS
38	SAR3	45/F	-	-	-	NIL RESPIR ATORY	RES	-	DD1,DD 2	DD4	-DO-	T/SAR	SARCOI DOSIS
39	SIL1	41/M	+	+	CRAMIC	5YRS	RES	-	DD2		SIL,SAR, LC,HP	CVD,IPF ,SIL,SAR ,INF	SILICOS IS
40	SIL2	54/M	+	+	SILICA	7YRS	RES	-	DD1,DD 2	DD4	-DO-	IPF,SIL, SAR,HP, INFECTI ONS	SILICOS IS
41	SIL3	49/M	+	-	SILICA	12YRS	RES	-		DD4	SIL,PMF	SIL,SAR IPF,CVD ,INF	SILICOS IS-PMF
42	SIL4	39/M	+	+	SILICA	4YRS	RES	-	DD1,DD 2		_DO_		SILICOS IS+PMF

43	SIL5	51/M	+	+	SILICA	10YRS	RES	-	DD1,DD2		T,SIL,TREATED LYMPHOMA,HISTOPLASMOSI	SAR,NSIP,HP,SIL INF	SILICOSIS
44	ABPA1	35/F	-	-	-	12YRS	OBS	NIL	DD1,DD2,DD3	DD7	ABPA,CYSTIC FIBROSIS	ABPA,CEP,CHURG-STRAUSS	ABPA
45	ABPA2	46/F	-	-	-	15YRS	OBS	NIL	DD1,DD2,DD3	DD7	ABOVE +AEP((?UCUS IMPCTION)	ABPA,CEP	ABPA
46	LC1	65/F	-	-	CHEMO/RT	15DAYS (COUGH)	RES	NIL	DD1,DD2		RP,LC,LIP,PE	CYTOLOGY+MALIGNANT CELLS	LC
47	LC2	61/F	-	-	CHEMO/RT	20DAYS (COUGH)	RES	NIL	DD1,DD2	DD4		SAME AS ABOVE	LC

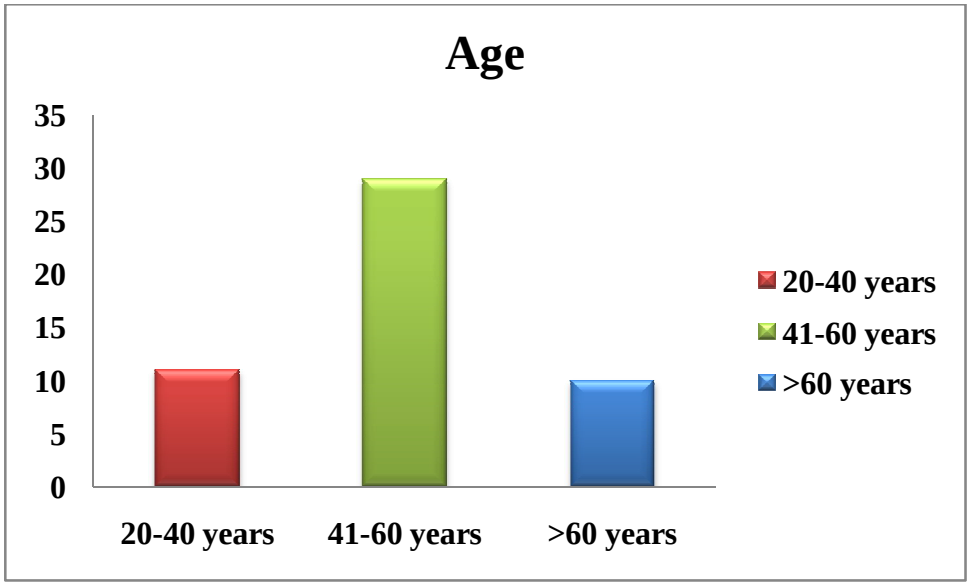
48	ARDS1	60/F	-	-	-	1WEEK	-	NIL	DD1,DD2	DD4	CXR-ARDS,VAP	ARDS,DAD,HP,INF	ARDS
49	ARDS2	44/M	-	-	-	1WEEK	-		DD1,DD2	DD4	CXR-ARDS,VAP	-DO-	ARDS
50	AB1	22/F	-	-	DRUGS_ANTIPSYCHOTICS	2YRS	-	NIL	DD1,DD2		CHRONIC ASPIRATION PNE,ENDBRONCHIAL TB,AB	SPIRATION PNEUMONIA,CD,INFECTIONS	ASPIRATION BRONCHIOLITIS

	AAD (MEAN YEARS)	MALE (%)	DURATION MEAN YEARS	DIAGNOSIS	TCC	AM	LY	NE	EOS	HIS
				NC						0
1	51.2	88.8	3.1	IPF	87	49	29	25	0	0
2	53.2	82.3	14.3	CHP	95	50	39	10	0	0
3	44.4	22.2	1.5	CVD	101	57	29	19	0	0
4	44.0	0	-	SAR	110	45	33	22	0	0
5	46.8	100	-	SIL	103	71	20	9	0	0
6	52	50	-	ARDS	340	38	25	37	0	0
7	40.5	0	3	ELD	90	48	17	7	29	0
8	63	0	45 DAYS	LC	100	59	25	16	0	0
9	20	0	2	AB	96	54	12	32	0	0
10	49	100	180 DAYS	PLCH	100	0	10	0	0	90

ABBREVIATIONS:

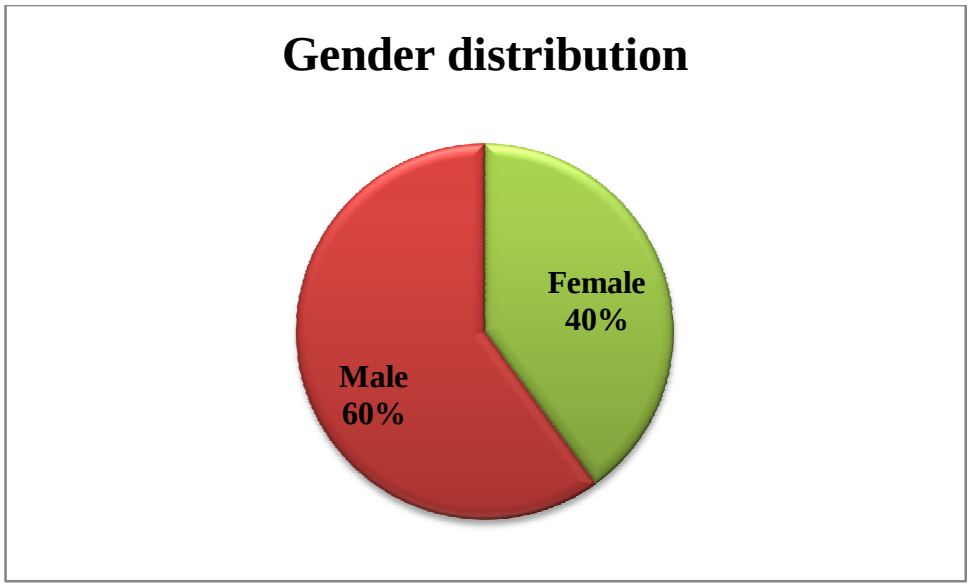
IPF- idiopathic pulmonary fibrosis, S-smoking, A-alcohol intake, Exp-exposure, D.O.I- duration of illness, PFT-spirometry, RES-restrictive, RHE-rheumatology diagnosis, RA-rheumatoid arthritis,SSc-systemic sclerosis, BAL1-bronchoalveolar lavage primary level dd, BAL2- bronchoalveolar lavage secondary level, CLI-clinical, AE-acute exacerbation, SAI- superadded infection, ALI-acute lung injury, BA-bronchial asthma, ELD- eosinophilic lung disease, INF-infection, ABPA-allergic bronchopulmonary aspergillosis, UIP-usual interstitial pneumonia, FIB-NSIP- fibrotic NSIP, CLN- centrilobular nodule,SSc -systemic sclerosis, PMF-progressive massive fibrosis, SIL- silicosis, SAR-sarcoidosis, CHP-chronic hypersensitivity pneumonitis, AHP-acute hypersensitivity pneumonitis, GGO- ground glass opacities, LC-lymphangitis carcinomatosis,AB-aspiration bronchiolitis

Age group	No
20-40 years	11
41-60 years	29
>60 years	10



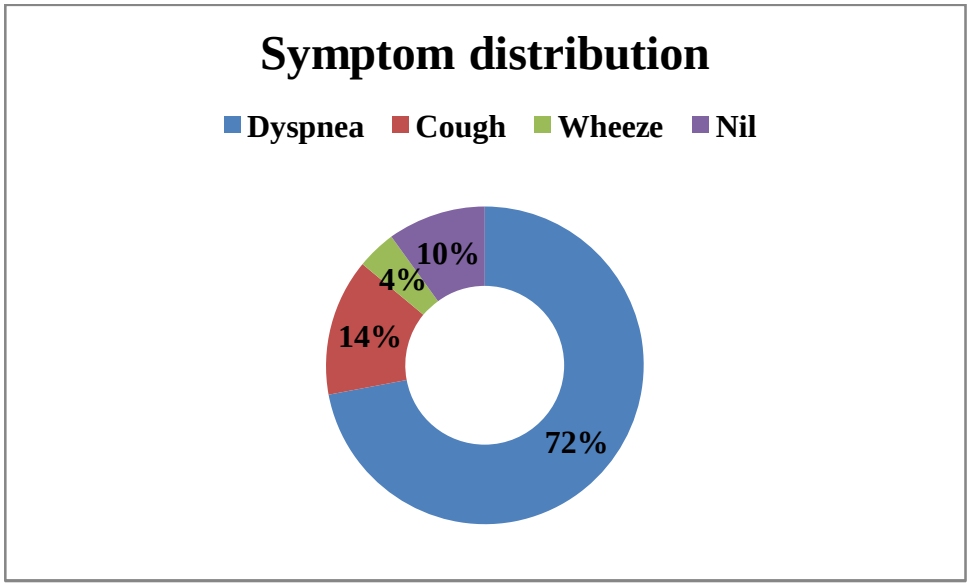
Out of 50 patients the above Graph shows the representation of age groups.

GENDER	NO
Female	20
Male	30



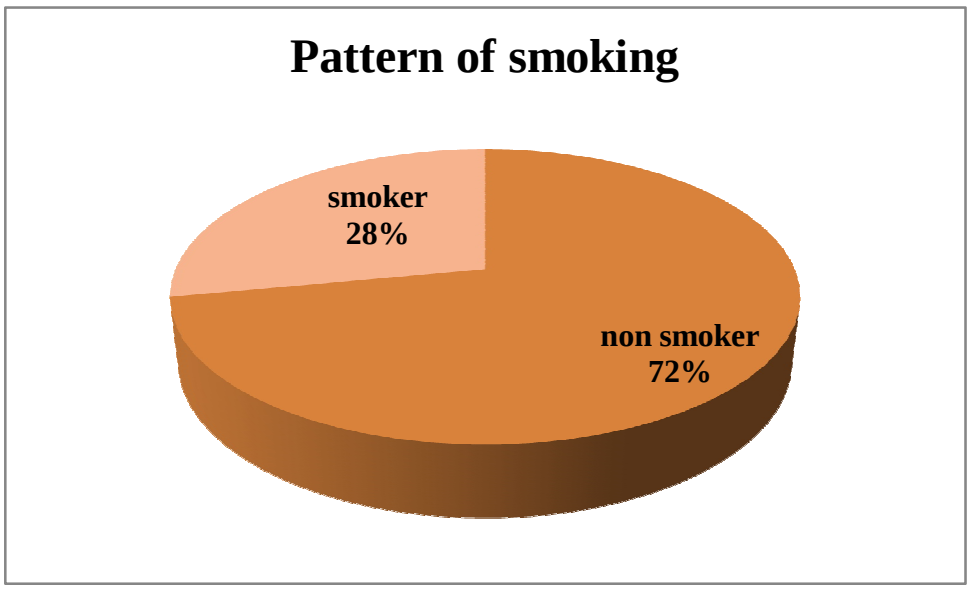
Out of 50 patients the above pie chart shows the gender distribution.

SYMPTOMS	NO
Dyspnoea	36
Cough	7
Wheeze	2
Nil	5



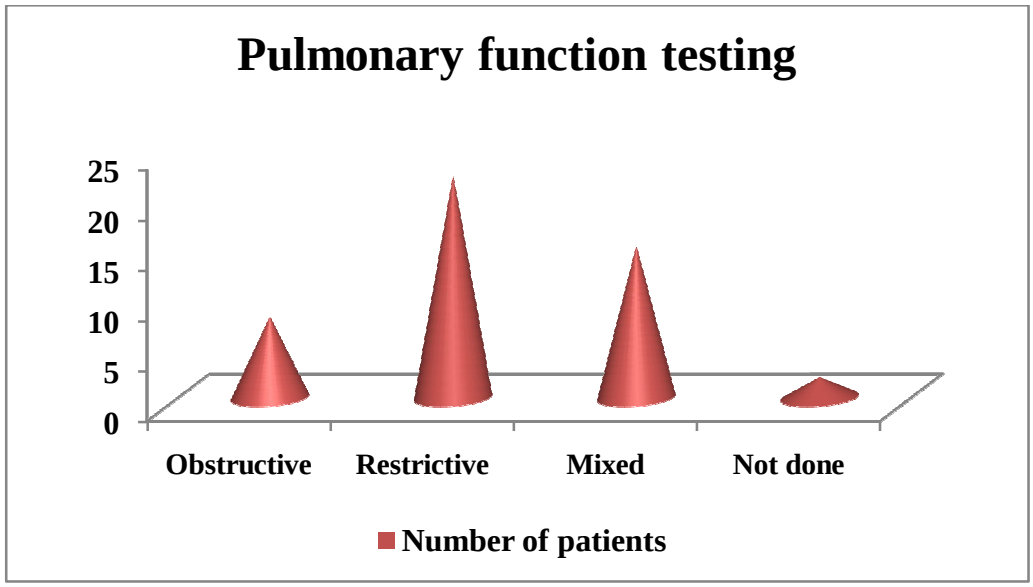
Out of 50 patients studied the predominant symptom was dyspnea.

Non smoker	36
Smoker	14



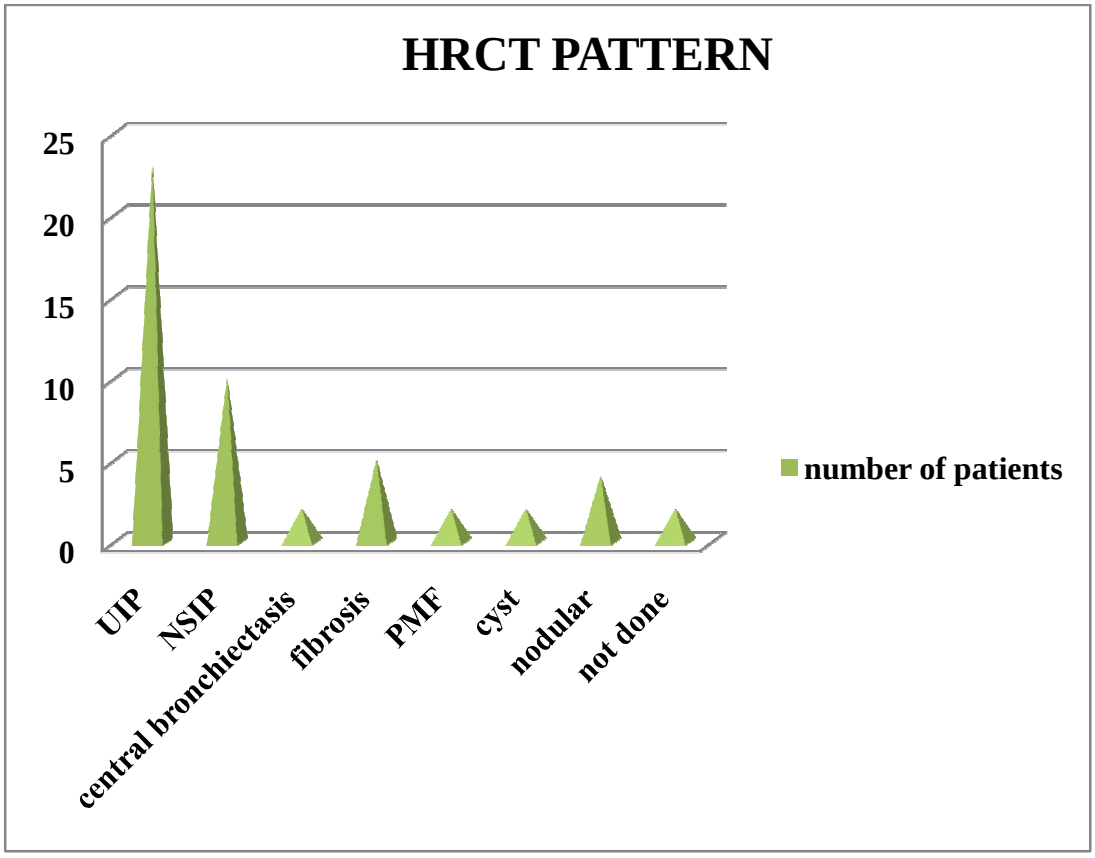
The above pie chart represents the distribution of smoking status of the patients studied.

PFT	Number of patients
Obstructive	8
Restrictive	22
Mixed	15
Not done	2
normal	3



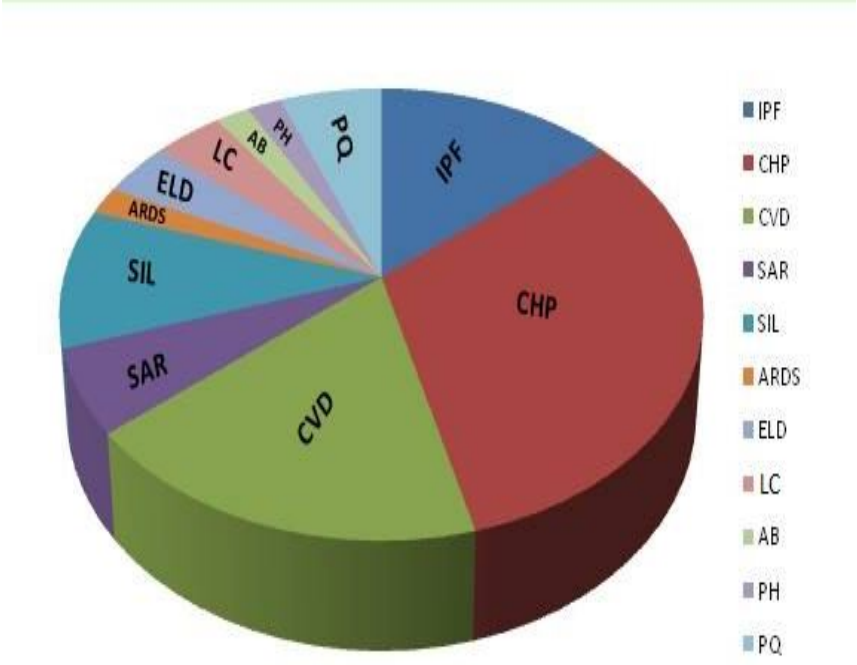
Out of the 50 patients studied the predominant pulmonary function testing pattern was restriction as shown above.

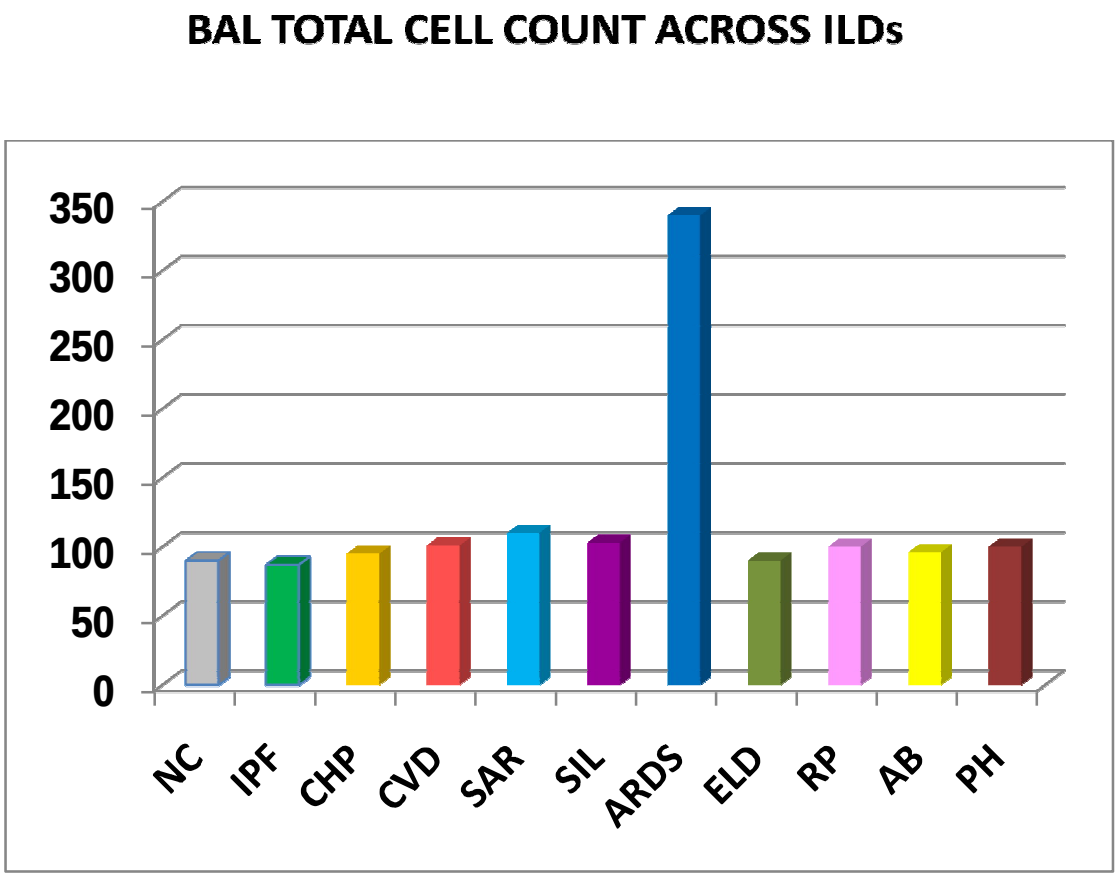
HRCT PATTERN	NO OF PATIENTS
Proximal bronchiectasis	2
Cystic	2
Fibrosis	5
Nodular	4
Not done	2
NSIP	10
UIP	23
PMF	2



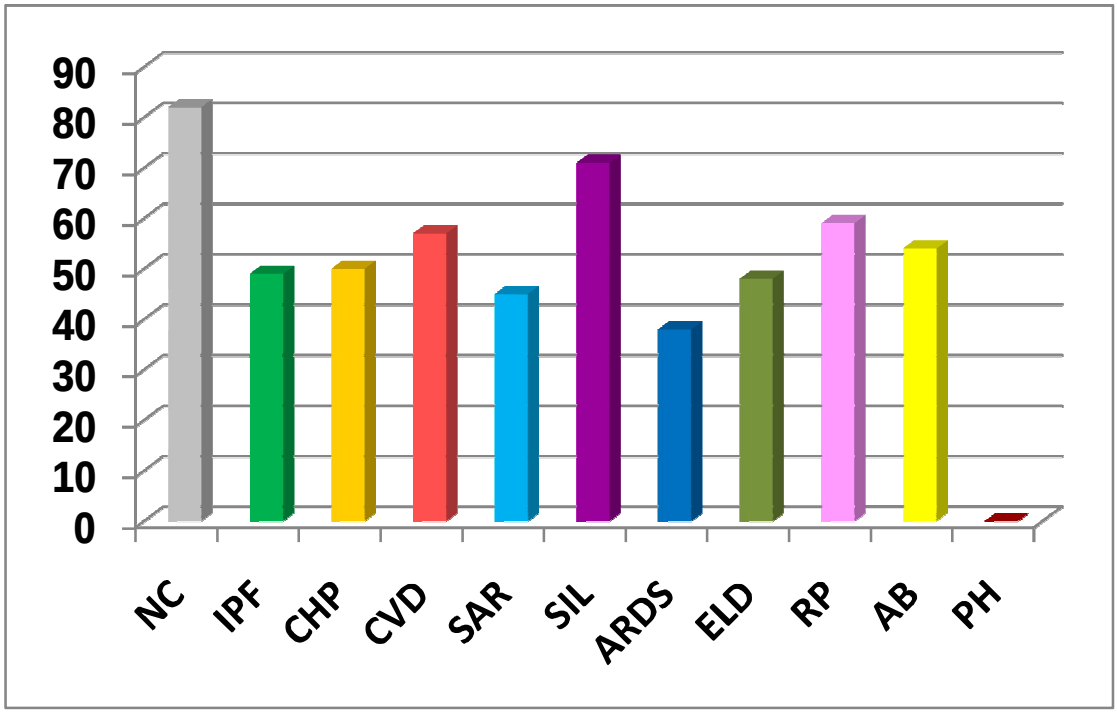
The above represents the distribution of the various HRCT patterns in the patients studied.

The distribution of the various ILDs are represented below

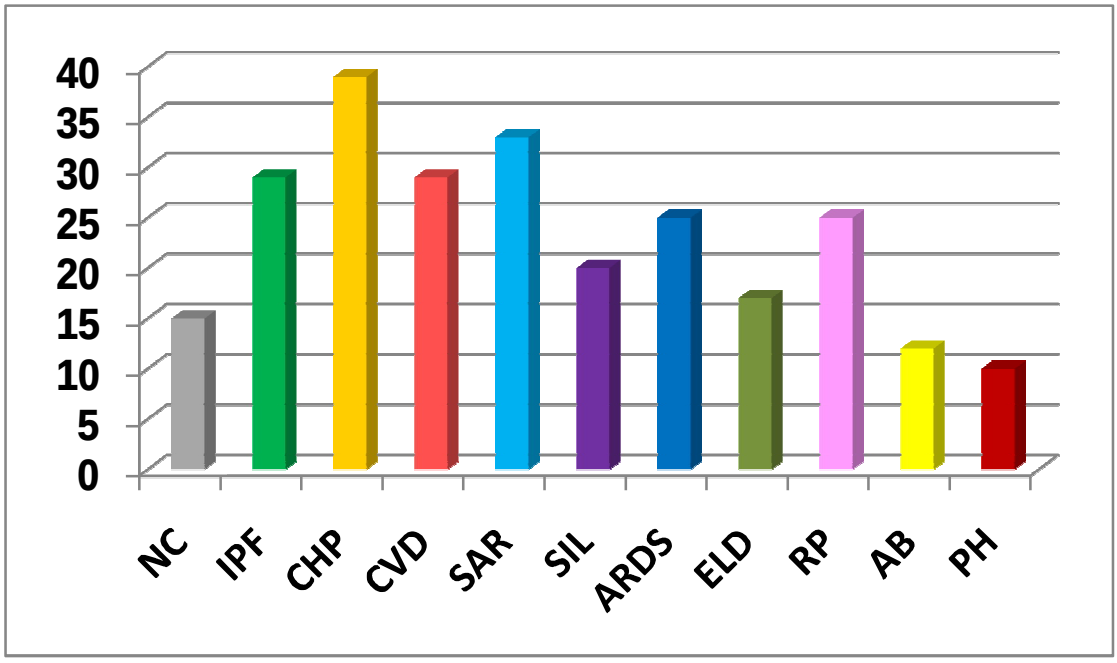




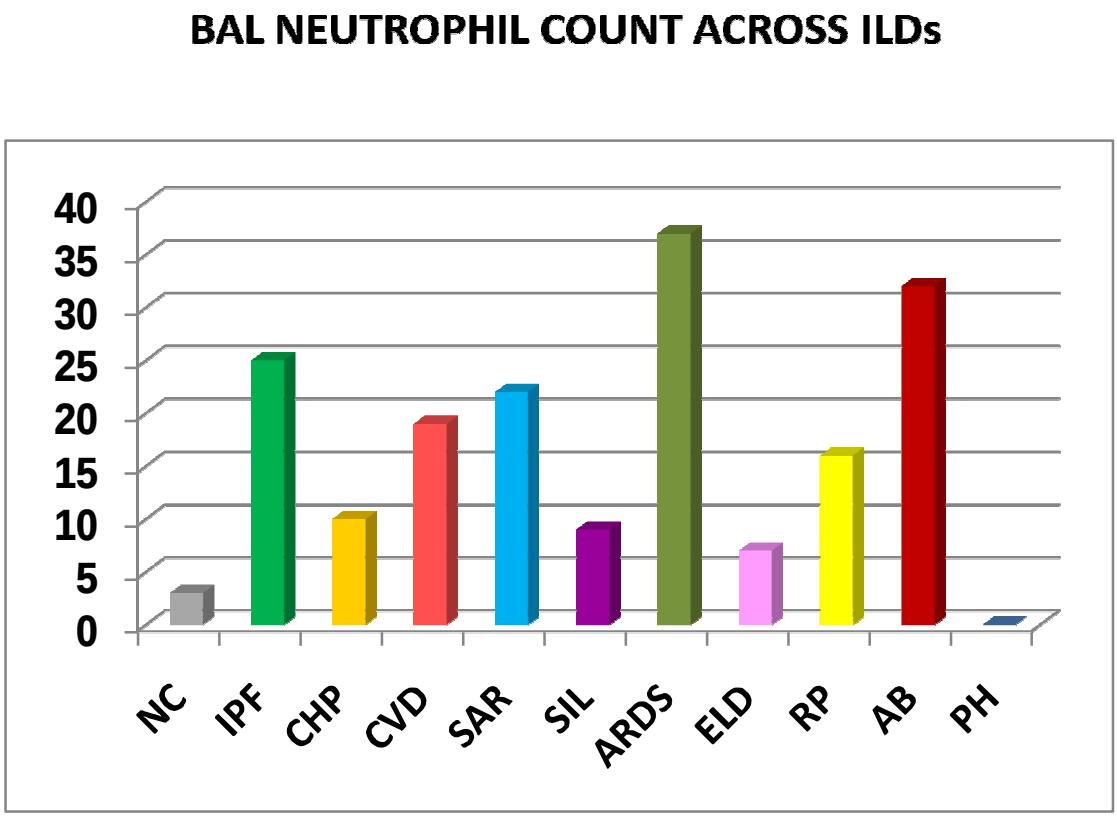
Among the 50 patients studied, the above graph represents the conditions showing total cell counts (BAL) in relation to the normal control (NC).



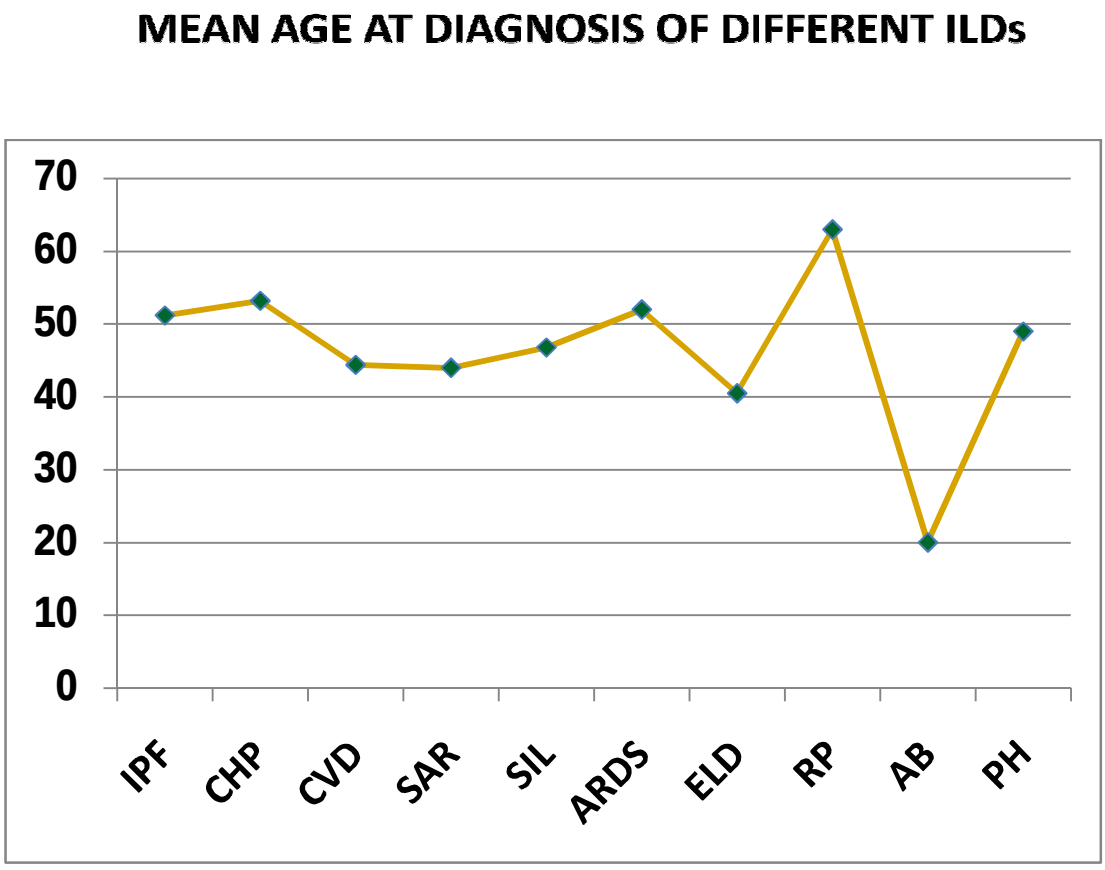
The above graph represents the Alveolar Macrophages levels in various ILDs in relation to the normal control.



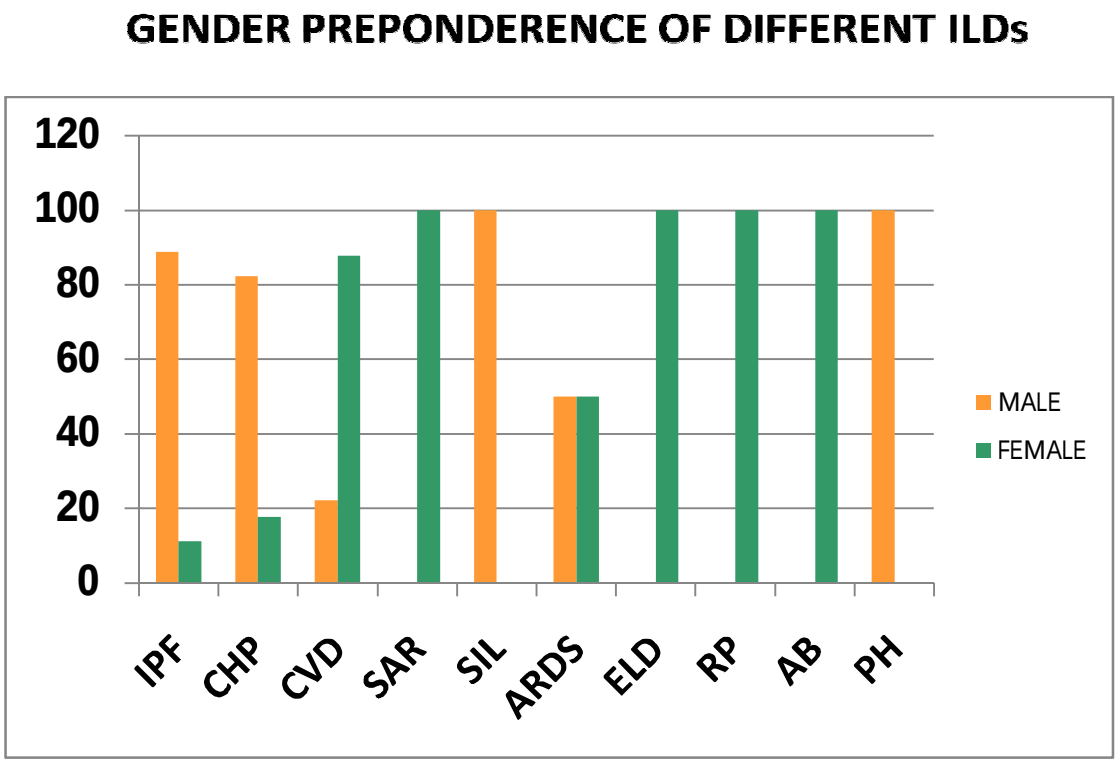
The above graph represents the BAL Lymphocyte variations in relation to the normal control values in different ILDs



The above graph shows neutrophil counts variations in relation to the normal control in various ILDs.



The above graph represents the mean age at Diagnosis of different ILDs



The above graph shows gender preponderance of different ILDs with silicosis being exclusive in males, IPF and CHP predominantly occurring in males. And sarcoidosis, CVD occurring more in females, in the population studied.

ABBREVIATIONS

IPF	-	Idiopathic Pulmonary fibrosis
CHP	-	Chronic hypersensitivity pneumonitis
CVD	-	Collagen Vascular Disease
SAR	-	Sarcoidosis
SIL	-	Silicosis
ARDS	-	Adult respiratory distress syndrome
ELD	-	Eosinophilic Lung Disease
RP	-	Lymphangitis Carcinomatosis
AB	-	Aspiration Bronchiolitis
PH	-	Pulmonary Histiocytosis

Lymphangitis carcinomatosis was seen in the 6th decade, IPF and CHP in 5th decade, ELD, CVD, SAR, and SIL were noticed in the 4th decade of life. The average duration of the disease was 3.1 years, 14.1 years and 1.5 years for IPF, CHP and CVD respectively.

The lymphocytes in lung secretions was significantly high in IPF, CHP, CVD and SAR while the percentage of neutrophils were significantly high in all the sub groups of ILDs noted in the cohort on comparison to normal values.

CHP- chronic hypersensitivity pneumonitis

CVD- collagen vascular disease/ CTD-ILD

SAR- sarcoidosis

SIL- silicosis

ELD- eosinophilic lung disease

IPF

Eight patients were diagnosed with IPF based on clinical evaluation, pulmonary function test(restrictive pattern) and HRCT findings(sub pleural/basal reticulation and honey comb appearance). The cell cytology of BAL on seven IPF patients revealed a lymphocyte count range of 25% to 38%, and neutrophil count range 12% to 52%. For those with a neutrophil count range less than 50%, a diagnosis of idiopathic pulmonary fibrosis with bronchitis probably superadded infection was made. A diagnosis of IPF with

Bronchitis and suppurative infection was made in one patient with a neutrophil count of above 50%. In patient 7 as the respiratory epithelial contamination was high and the analysis was forbidden due to sub optimal sample.

CHP

Out of 17 patients diagnosed with chronic hypersensitivity pneumonitis, patient CHP11 was not analysed due to suboptimal quality(PQ-poor quality)identified based on epithelial cells levels i.e. More than 5 percent. In the rest of the samples, the lymphocyte count range was 26% to 55% and the neutrophil count was in the range of 5% to 20%. Based on the cellular count, a diagnosis of acute exacerbation of

chronic hypersensitivity pneumonitis with bronchitis probably associated with superadded infection was made in all these patients. In addition to the above findings, patient 10 had 3% eosinophils, which redefined the diagnosis as acute exacerbation of chronic hypersensitivity pneumonitis with allergic bronchitis probably associated with superadded infection.

CVD

The lymphocyte range was 8% to 70% while the neutrophil count was in the range of 8% to 65% in nine patients. In patient CVD-1 as the lymphocyte count was 70% a diagnosis of acute exacerbation of interstitial lung disease with bronchitis probably associated with superadded infection was made. In patient CVD-2 with rheumatoid arthritis and a neutrophil count above 50% in the BAL cellular pattern, the diagnosis was refined as rheumatoid arthritis associated interstitial lung disease with bronchitis and suppurative infection. In the rest of the patients the diagnosis was refined as rheumatoid arthritis with interstitial lung disease with bronchitis probably due to with superadded infection.

EOSINOPHILIC LUNG DISEASE:

Apart from the routine lymphocyte and neutrophil count, eosinophil count of more than 25% was diagnostic of acute/chronic eosinophilic pneumonia and ABPA.

PULMONARY HISTOCYTOSIS:

Predominance of histocytosis BAL fluid was able to narrow down this diagnosis. sarcoidosis:In three patients with sarcoidosis, the lymphocyte and neutrophil count range was 28% to 32% and 10% to 45% respectively. Based on BAL finding the previous diagnosis was refined as sarcoidosis induced interstitial lung disease with bronchitis probably associated with superadded infection.

ARDS AND ASPIRATION BRONCHIOLITIS

These diseases were diagnosed based on clinical history and examination and the role of BAL in defining the diagnosis was limited.

Lymphangitis carcinomatosa: BAL cytology yielded the diagnosis and made a biopsy unnecessary, in both the cases.

Overall, BAL findings were able to clinch the diagnosis in eosinophilic pneumonia, lymphangitis carcinomatosis and pulmonary histocytosis, while it refined the diagnosis of IPF and CHP.BAL helped in establishing infection as the cause of acute exacerbation in IPF,and in other ILDs. On the other hand, the role of BAL findings in sarcoidosis and silicosis was limited as HRCT had precisely help to diagnose the disease based on the image pattern. BAL had no role to play in the diagnosis of ARDS and aspiration bronchiolitis as the diagnosis is more on clinical history and evaluation.

STATISTICAL SIGNIFICANCE:

Statistically significant increase in the different cell counts were obtained for the following ILDs after comparison with normal cell counts; ARDS: alveolar macrophages($p=0.018$), CHP: neutrophils($p=0.01$), ELD: mast cells($p=0.000$). A statistically significant decrease in the lymphocytes was noticed in ARDS($p=0.001$)

DISCUSSION

Usefulness of the clinical diagnostic test is graded based on its sensitivity, specificity, invasiveness, reproducibility and its contribution to the diagnosis of the disease. Based on these factors, new diagnostic tests for disease are invented and the old test wane of with time. Interestingly, as the pathogenesis of disease unwinds with time there may be need of multiple clinical tests to make precise diagnosis and to improve the management strategy. Under these situations, it may be difficult to conceive that an old test for a particular disease that has been used in the past may have new potential uses in modern medicine.

Bronchoalveolar lavage(BAL) is now widely accepted as a safe procedure to sample alveolar secretions for studying cellular and acellular components for diagnostic purpose [106-111]. Bronchoscopy and BAL was once thought to hold a great scope in diagnosing and managing ILD. With time it came to understand, that though BAL immune cell features often had characteristics that were highly consistent with several forms of ILD, BAL cell profiles or soluble components could not reliably make a definite diagnosis in several forms of ILD if used as a standalone test of diagnosis. The evaluation of interstitial lung disease based on BAL findings was typically nonspecific, being consistent with or suggestive of a given condition, rather than pathognomonic, BAL data were subject to

considerable variability, and the potential number diseases are much more than the number of safely discernible cellular patterns. This, only in rare instances, the data lead to a unique conclusion; in the majority of cases, BAL cell differentials are only able to render some diagnoses more likely and to exclude others with some probability. This uncertainty, in combination with differences in clinical setting and experience, resulted in different opinions about the diagnostic value of BAL among clinicians.

In early 1990s, HRCT came into widespread clinical use. As HRCT imaging patterns were consistent with specific forms of ILD such as IPF or sarcoidosis, the likelihood of making a diagnosis was high. Despite the acceptance of obtaining HRCT scan during the initial stages of patients with ILD, many patients with new onset ILD may not have the characteristic patterns that allow a diagnosis to be made with a high level of confidence by HRCT imaging alone. However, when clinical informations and HRCT findings were combined with BAL fluid analysis, confident diagnosis may emerge that obviate the need for surgical lung biopsy. Although the BAL cell pattern can provide useful information of the specific ILD diagnosis, this would be possible only if the bronchoscopist uses the appropriate technique to obtain the fluid, and the differential cell count is performed according to good clinical laboratory practice by personnel with adequate experience BAL

cytological analysis and interpreted by an expert familiar with the diverse spectrum of specific forms of ILD[114,115]. With this in mind the present study utilized the recommendations and guidelines of ATS concerning the use of BAL in the diagnosis and management of patients with suspected ILD. Based on the cellular pattern obtained we were able to fit the differential diagnosis of 47 patients within the classification provided by ATS. We were also able to find inappropriate BAL procedure in rest of the three patients. Later we made diagnosis of different ILDs based on clinical examination, HRCT findings and BAL cell pattern separately. And then with all the three modes of assessment. When a clinical diagnosis was combined with HRCT the differential diagnosis was narrowed down to minimum of two diseases. Considering BAL cellular pattern along with clinical examination and HRCT findings not only narrowed the type of ILD but also enhanced the diagnosis for better management strategy. The enhancement in the diagnosis included stability of the disease, acute or chronic nature of the disease and probable cause for acute exacerbation. This leaves the physician to take an appropriate decision to treat the cause of acute exacerbation along with the primary aetiology or to treat the primary cause alone. Thus, this multiple assessment strategy was able to treat patients appropriately with much more precision and accuracy.

In patient1 an IPF suspected patient HRCT had provided four differential diagnosis of IPF, CHP, asbestosis, sarcoidosis and CVD based on honeycoomb appearance. The clinical findings and BAL analysis suggested four differential diagnosis namely IPF, NSIP, acute lung disease and suppurative infection. Combining clinical, HRCT and BAL findings, the diagnosis was refined as acute exacerbation of idiopathic pulmonary fibrosis with bronchitis and probably associated with superadded infection. This had helped the clinician to treat the infection to control the acute episode. In patient 8, HRCT listed the differential diagnosis similar to that of patient 1 based on cystic changes honey comb appearance, but BAL clearly demonstrated predominance of histocytes in the lung secretion to narrow down the diagnosis as pulmonary histocytosis. This changed the modality of treatment in this patient.

In patient 10, with a clinical diagnosis as ILD, HRCT revealed bilateral upper lobe fibrosis with traction bronchiectasis. Adding BAL input redefined the diagnosis as sub acute exacerbation of CHP associated with non infectious bronchitis based on the lymphocyte and neutrophil counts. On the other hand, patient 12 had a neutrophil count more than 50% in the cellular pattern that gave a diagnosis of acute exacerbation of CHP with bronchitis and suppurative infection. In eosinophilic

pneumonitis BAL played a very important role in assisting clinical and HRCT findings to clinch the diagnosis. In some of the ILDs such as the sarcoidosis, silicosis, ILD associated with collagen vascular diseases HRCT stands as the important test along with clinical examination in determining the diagnosis. In all these diseases BAL was helpful to predict the acute/ sub acute or chronic nature of the disease and the association of infection. Whereas in ARDS the clinical criteria along with x ray chest was adequate to make a diagnosis.

Thus the present study was able to demonstrate that BAL done as per the guidelines of ATS may act as an important test along with clinical and HRCT findings for a proper diagnosis in some ILDs, while in others, HRCT was found to be very successful in predicting the diagnosis, BAL assist in predicting the acute/chronic nature of the disease and gives the hint on the superadded infection status that would help in proper management. Thus BAL may be a routine test in eligible ILD patients along with clinical evaluation and HRCT.

CONCLUSIONS

- BAL cellular profile obviates the need for surgical lung biopsy in certain ILDs namely lymphangitis carcinomatosis, Eosinophilic lung diseases and Langerhans cell histiocytosis.

- BAL cellular profile could be supportive of diagnosis in the presence of clinical and radiological features typical of a specific ILD

- BAL plays an important role in establishing infection as the cause of an acute exacerbation of ILD. If infection is not established, guides the clinician to look for an alternate cause such as a thromboembolic event or a left heart failure

BAL cellular analysis has documented the presence of inflammatory cells in asymptomatic patients with HRCT evidence of early ILD, which could predict an exacerbation in the near future.

- BAL is a relatively safe procedure, and maybe a routine test in ILD(in the absence of contraindications to bronchoscopy), along with clinical evaluation and HRCT

STUDY LIMITATIONS

- Sample size was small
- This study did not include all types of ILDs, namely Cryptogenic Organising Pneumonia, Acute Interstitial Pneumonias, Drug induced ILDs to name a few.

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PROTOCOL (DETAILED DESCRIPTION)

1. Title

Bronchoalveolar lavage (BAL) Cellular Analyses as a Diagnostic Intervention for Patients with Suspected ILD in conjunction with HRCT Imaging

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2. OBJECTIVE (S) / AIM

Primary Objective

To optimize the Brochoalveolar Lavage (BAL) procedure as per the recommendations put forth by the American Thoracic Society for the cellular analysis of interstitial lung diseases.

Secondary Objectives

- Optimization of the BAL procedure as per the recommendations of the American Thoracic Society
- BAL cellular analysis association with clinical characteristics of different interstitial lung diseases and their radiological/pathological findings.

3. INTRODUCTION

Bilateral parenchymal infiltration of lung tissue is called interstitial lung disease (ILD). It can present as an acute or chronic condition with variable degree of inflammation and fibrosis. The condition is immune mediated where infection and neoplasm do not play a role in the etiology of the disease. ILDs are generally characterized clinically by exertional dyspnea, bilateral pulmonary infiltrates on thoracic imaging, abnormal pulmonary physiology, and abnormal gas transfer. They are characterized pathologically by an accumulation of inflammatory and immune effector cells that is often accompanied by abnormal extracellular matrix in the distal airways, alveolar walls, and interstitium.

Chronic ILDs usually evolve over months to years and include disorders of both known and unknown causes. Among the ILDs with known causes or associations are the pneumoconioses, ILD associated with connective tissue disease (CTD-ILD), and hypersensitivity pneumonitis (HP). Among the ILDs of unknown cause are sarcoidosis and idiopathic interstitial pneumonias (IIP). Idiopathic interstitial pneumonia (IIP) includes idiopathic pulmonary fibrosis (IPF), nonspecific interstitial pneumonia (NSIP), desquamative interstitial pneumonia (DIP), respiratory bronchiolitis with interstitial lung disease (RBILD), acute interstitial pneumonia (AIP), cryptogenic organizing pneumonia (COP), and lymphoid interstitial pneumonia (LIP).

Bronchoalveolar lavage has been used evaluate patients with suspectedILD to identify the specific type of ILD. Advent of high resolution computed tomography (HCRT) has reduced the clinical utility of BAL. HRCT can noninvasively identify specific imaging patterns that may be virtually diagnostic or strongly support certain forms of ILD. This has greatly improved the clinician's ability over the past decade to narrow the differential diagnosis. As a result, a likely diagnosis is determined in the majority of cases (1–3). The widespread use of HRCT to evaluate patients with ILD has reduced the need for invasive diagnostic procedures, although sampling is still performed to confirm or secure an accurate diagnosis. Diagnostic sampling is also performed when there is ongoing clinical suspicion of ILD despite a normal HRCT (i.e., occasionally patients whose HRCT was interpreted as normal have evidence of ILD on BAL or lung biopsy). Following the initial clinical andradiographic evaluation of patients presenting with suspected ILD, BAL cellular analysis may be a useful adjunct in the diagnostic evaluation of individuals who lack a confident usual

interstitial pneumonia (UIP) pattern on high-resolution computed tomography (HRCT) imaging of the thorax.

BAL is one sampling technique. It samples the cellular and acellular components of distal bronchioles and gas exchange units. BAL analysis is seldom diagnostic by itself, but BAL cell pattern results may support a diagnosis and/or narrow the differential diagnosis when considered in the context of the medical history (e.g., occupational and environmental exposures, drug ingestion, prior radiation therapy), physical examination (e.g., extrapulmonaryabnormalities), and radiologic findings (e.g., HRCT findings). The usefulness of BAL cell profiles is the subject of ongoing debate and controversy because its findings are hampered by poor sensitivity and specificity (4). In addition, a normal BAL differential cell profile does not exclude the presence of microscopic abnormalities in lung tissue. The clinical utility of BAL in identifying the cause of ILD is proven, provided the technique is performed correctly, BAL fluid be handled and processed properly. Recently, the American Thoracic Society (ATS) clinical practice guideline provides a comprehensive, conceptually balanced, and evidence-based perspective on the clinical utility of BAL cellular analysis for the evaluation of suspected ILD. These guidelines will increase the utility of BAL in the diagnostic evaluation of ILD and promote the use of BAL in clinical of ILD so that future guidelines may be based upon higher quality evidence.

The present work would utilize the recommendations put forth by the ATS to optimize the BAL procedure and associate the finding across different clinical entities of ILD including HRCT. In addition, the study would also associate BAL findings with lung tissues procured through transbronchial biopsy in subset of patients for

whom biopsy is warranted (5).This may facilitate future clinical studies in patients with suspected ILD, which investigate potential biomarkers in BAL that may predict prognosis and response to therapeutic interventions for ILD.

4.METHODOLOGY (MATERIALS & METHODS)

Subject Selection

Seventy five ILD patients will be enrolled for the study based onclinical and radiological evaluation after institutional ethics committee approval. 15 ml of peripheral blood would be collected from the patients after obtaining informed consent for the study. The blood samples will be utilized for routine blood investigations, disease specific investigations and for genetic analysis.

Inclusion Criteria

- ILD patients diagnosed based on clinical and HRCT findings
- Acute and chronic ILDs in immunocompetentpatients.
- ILD patients tolerable to the procedure.
- Patients above 18 years of age.
- Patients with ability and voluntarily signs the informed consent.

Exclusion Criteria

- ILD patients without HCRT diagnosis
- ILD patient with immunodeficiency
- ILDs associated with infection or neoplasm
- ILD patients with bleeding tendency.
- Pediatric patients
- Pregnant women

Screening Procedures / Visits:

1. BAL is performed with the fiberoptic bronchoscope in a wedge position within the selected bronchopulmonary segment. The total instilled volume of normal saline should be no less than 100 ml and should not exceed 300 ml. Three to five sequentially instilled aliquots are generally withdrawn after each aliquot instillation (6).
2. For optimal sampling of distal airspaces, the total volume (pooled aliquots) retrieved should be greater than or equal to 30% of the total instilled volume. A total volume of retrieved fluid less than 30% may provide a misleading cell differential, especially if total retrieved volume is less than 10% of total instilled volume. If less than 5% of each instilled aliquot volume is recovered during the procedure due to retention of most of the fluid in the lavaged segment, the procedure should be aborted to avoid increased risk of tissue disruption and/or inflammatory mediator release due to overdistention of the lavaged segment.
3. A minimal volume of 5 ml of a pooled BAL sample is needed for BAL cellular analysis. The optimal volume is 10 to 20 ml. It is acceptable to pool all aliquots of the retrieved BAL fluid for routine analyses (including the first retrieved aliquot).
4. BAL cell differential counts with greater than 15% lymphocytes, greater than 3% neutrophils, greater than 1% eosinophils, and greater than 0.5% mast cells represent a lymphocytic cellular pattern, neutrophilic cellular pattern, eosinophilic cellular pattern, and mastocytosis, respectively. Each has diagnostic implications.
5. A predominance of macrophages containing smokingrelated inclusions with no or minor increases in other cell types is compatible with smoking-related ILD such as desquamative interstitial pneumonia (DIP), respiratory bronchiolitis interstitial lung disease (RBILD), and
Langerhans cell histiocytosis.

I. PRE-PROCEDURE PREPARATION

Patients with suspected ILD for whom the clinician is considering BAL should undergo routine clinical evaluation before the procedure. This evaluation, which

includes inquiry and appropriate testing for bleeding tendencies, is intended to minimize the likelihood of procedure-related complications by identifying potential risk factors that can be corrected or mitigated in advance. Once it is confirmed that the patient is a suitable candidate forBAL, the procedure may be scheduled.

Recommendation 1.

For patients with suspected ILD in whomit has been decided that a BAL can be tolerated and will beperformed, we suggest that the BAL target site will be chosen onthe basis of an HRCT performed before the procedure, ratherthan choosing a traditional BAL site (i.e., the right middle lobe or lingula). HRCT can be useful for identifying target areas of the lungthat are most likely to provide diagnostic specimens when samplingvia BAL. Generally, areas of alveolar ground glass opacity, more prominent nodular profusion, or fine reticulation are likely to provide optimal targets. Target areas as well as characteristics of parenchymal abnormalities may change with time and, therefore, the HRCT should not be performed too far in advance of the BAL procedure. Although there are no controlled clinical trials that have compared whether BAL sites identified by HRCT yield more useful information than traditional BAL sites (i.e., easily accessible sites that provide a good volume of return such as the right middle lobe or lingula), some reports suggest that HRCT may be useful for choosing a site of lavage.

II. THE BAL PROCEDURE

During standard flexible bronchoscopy, the bronchoscope is placed in a wedge position within the selected bronchopulmonarysegment. Normal saline (at room temperature) is instilledthrough the bronchoscope, with a total volume that is between 100 and 300 ml and divided into three to five aliquots. After the instillation of each aliquot, instilled saline is generally retrieved using a negative suction pressure less than 100 mm Hg. The negative suction pressure should be adjusted to avoid visible airway collapse. The minimal total volume retrieved should be greaterthan or equal to 5% of the instilled volume (optimal samplingretrieves >30%). If less than 5% of each instilled aliquot volume is recovered during the procedure due to retention of most of

the fluid in the lung, the procedure should be aborted to avoid increased risk to the patient. A minimal volume of 5 ml of a pooled BAL sample is needed for BAL cellular analysis (the optimal volume is 10–20 ml); it is acceptable to pool all aliquots of the retrieved BAL fluid for routine analyses. Occasionally, the gross appearance of the BAL fluid will provide diagnostic clues. For example, grossly bloody BAL fluid that returns with increasing intensity in sequential aliquots indicates acute diffuse alveolar hemorrhage, while grossly cloudy (i.e., milky or light brown-beige color) BAL fluid that returns with flocculent material that settles by gravity to the bottom of the container within 15 to 20 minutes of fluid retrieval is highly suggestive of pulmonary alveolar proteinosis (PAP).

III. HANDLING OF THE BAL FLUID

The BAL fluid should be collected in containers that do not promote cell adherence to container surfaces (e.g., silicone coated glass or polypropylene or other plastics that are designed for suspension tissue culture). Its method of transport then depends upon how long it is anticipated that it will take to reach the analytical laboratory. The specimens will be transported at 4°C (i.e., on ice). If a delivery time greater than1 hour is anticipated, then transport in the original lavage saline is discouraged. Instead, the cells should be centrifuged at a speed that maintains cellular integrity (e.g., 250–300 3 g for 10 min) and then resuspended in a nutrient-supplemented medium (e.g., MEM125mM HEPES or RPMI 1640125mM HEPES) and stored at 4°C, where they may remain for up to 24 hours. If a centrifuge is not available, MEM or RPMI may be added to the pooled lavage sample with subsequent storage at 4°C for up to 12 hours, but the sample will be transported to the laboratory as soon as possible and a prolonged interval between BAL fluid retrieval and laboratory processing is discouraged. BAL fluid will not be frozen or transported with dry ice.

IV. PROCESSING

Prompt processing of the BAL fluid or cell suspension once it reaches the laboratory provides optimal results. Labware will be used that does not promote cell

adherence to container surfaces. Specimens with gross mucus can be strained through loose gauze, or small amounts of mucus can be dissolved with dithiothreitol, if necessary. The specimen will then be centrifuged at an appropriate speed, resuspended, and analyzed. BAL fluid that is not going to be analyzed immediately will be centrifuged, the cell pellet resuspended in a nutrient supplemented medium, and then refrigerated at 48C for up to 24 hours. Cells that were already suspended in a nutrient supplemented medium due to delayed transport can simply be refrigerated at 4°C. Specimens obtained more than 24 hours before are not suitable for analysis.

V. BAL CELLULAR ANALYSIS IN THE DIAGNOSIS OF SPECIFIC ILD

A variety of diagnostic studies may be performed on BAL fluid. In patients with suspected ILD, typical diagnostic studies are a differential cell count, microbiological studies (to screen for mycobacterial and fungal disease), and cytopathology.

Recommendation 2.

For patients with suspected ILD who undergo BAL, a differential cell count be performed on the BAL fluid. This includes lymphocyte, neutrophil, eosinophil, and mast cell counts. The remaining sample may be used for microbiological, virological, and/or malignant cell cytology laboratory testing, if clinically indicated. The reason for routine cellular analysis whenever BAL is performed in a patient with suspected ILD is that identification orexclusion of a predominantly inflammatory cellular pattern (increased lymphocytes, eosinophils, and/or neutrophils) maysupport a specific type of ILD or help narrow the differential diagnosis, when considered in the context of the clinical and radiological findings. The notion that a prominence of specific nucleated inflammatory or immune cells in the BAL correlates with an increased likelihood of certain types of ILD is supported by numerous accuracy studies that are limited by risk of bias. These include pronounced BAL eosinophilia in eosinophilic pneumonia (7, 8) or drug reactions (9–11), and BAL lymphocytosis in

sarcoidosis (12–15), hypersensitivity pneumonitis (16–18), pneumotoxic drug reactions (19, 20), or cellular NSIP (21, 22).

Follow up Procedures / Visits:

The patient will be observed for 48 hours for post procedure bleed at the in-patient ward before discharged with care.

Assessments of Parameters

TECHNIQUE OF BAL CELL ANALYSIS

The cellular analysis will be performed within 1 hour if the BAL fluid is in nutrient-poor media (e.g., saline) or within 2 to 3 hours for optimal results if the BAL fluid is in a nutrient-supplementedmedium. The total cell count (nucleated immune cells) is usually obtained via a hemocytometer, and cell viability is determined by Trypan blue exclusion. Differential cell counts will be performed via cytocentrifugation with staining (Wright-Giemsa or May-Grunwald-Giemsa) and enumeration of at least 400 cells. The presence and relative numbers of erythrocytes and epithelial cells should be noted. The presence of squamous epithelial cells suggests that BAL fluid is contaminated with upper airway secretions, and the presence of large numbers of bronchial epithelial cells suggests that the BAL may not have adequately sampled distal airspaces. Excess BAL fluid will be stained and cultured for mycobacteria and fungi in the microbiology laboratory, as well as screened for neoplastic cells. These are important additional tests to consider because infections and diffuse neoplasms can masquerade as ILD or coexist with ILD.

INTERPRETATION OF BALL DIFFERENTIAL COUNTS

The ranges of differential cell counts that are considered normal and abnormal derive from several sources. Numerous investigators have published BAL immune cell profiles from cohorts of clinically normal volunteer subjects recruited in single-center studies (22–28) and these reports have been used to define normal and abnormal differential cell counts. In addition, the multi-center BAL Cooperative Study (22) reported the differential cell counts in the BAL of normal subjects

(including smokers or ex-smokers) compared with patients with ILD. An increased number of nucleated immune cells and abnormal proportions of immune cell types may suggest or support specific types of ILD in the absence of an infection. A mixed cellular pattern can be observed with any ILD; when mixed cellular patterns are observed, the dominant cell type may be the most consistent with a specific ILD diagnosis. A BAL fluid cell differential count with greater than 15% lymphocytes, greater than 3% neutrophils, greater than 1% eosinophils, or greater than 0.5% mast cells indicates BAL lymphocytosis (i.e., a lymphocytic cellular pattern), BAL neutrophilia (i.e., a neutrophilic cellular pattern), BAL eosinophilia (i.e., an eosinophilic cellular pattern), or BAL mastocytosis, respectively. A lymphocyte differential count greater than or equal to 25% suggests granulomatous lung disease (e.g., sarcoidosis, HP, NSIP, chronic beryllium disease, drug reaction, LIP, COP, or lymphoma), while a lymphocyte differential count greater than 50% is particularly suggestive of HP or cellular NSIP. An eosinophil differential count greater than or equal to 25% is virtually diagnostic of eosinophilic lung disease in the appropriate clinical setting. A neutrophil differential count greater than or equal to 50% strongly supports acute lung injury, aspiration pneumonia, or suppurative infection. Finally, a mast cell differential count greater than 1% combined with a lymphocyte differential count greater than 50% and a neutrophil count greater than 3% is suggestive of HP. A predominance of macrophages containing smoking-related inclusions with no or minor increases in other cell types is compatible with smoking-related ILD, such as DIP, RBILD, or pulmonary Langerhans cell histiocytosis (PLCH). Additional tests to identify and count Langerhans cells in the appropriate clinical setting may be useful in narrowing the differential diagnosis. A predominance of hemosiderin-laden macrophages is suggestive of chronic or occult alveolar hemorrhage syndromes resulting in pulmonary hemosiderosis or diffuse alveolar damage.

Recommendation 3.

For patients with suspected ILD in whom BAL is performed, the lymphocyte subset analysis NOT be a routine component of BAL cellular analysis. The lymphocyte subset analysis (by cytometry or immunocytochemistry) will not be performed routinely, but rather would be performed if a lymphocytic disease is

suspected or the initial BAL cellular findings identify a lymphocytosis. This suggestion is based upon the committee'sclinical experience that lymphocyte subset analysis is rarely helpful and potentially misleading in the absence of a clinically suspected lymphocytic disease or a lymphocytosis. Many investigators have characterized lymphocyte subsets on the basis of T helper (CD41) versus T suppressor (CD81) phenotypes, and have found correlations of the CD41/CD81T lymphocyte ratio with specific disease processes such as sarcoidosisand hypersensitivity pneumonitis (16,17,29,30). However, subsequent investigations have found that the CD41/CD81 ratio may not be significantly increased in a substantial number of patients with sarcoidosis (31,32) or significantly decreased in a substantial proportion of patients with hypersensitivity pneumonitis (33,34), and can change during the course of the disease process. In addition, the BAL CD41/CD81T lymphocyte ratio varies with age and may be significantly increased in normal subjects (35). These issues are discussed extensivelyin the portion of the online supplement that pertains to specific forms of ILD. However, in the case of sarcoidosis, the combination of BAL lymphocytosis combined with a considerablyincreased BAL CD41/CD81 lymphocyte ratio (e.g., >4) may increase the confidence of a diagnosis of sarcoidosis if other clinical features and imaging are consistent with this diagnosis, and lymphocyte subset determinations may be performed at the discretion of the pulmonologist if such analysis can be reliably performed in the clinical laboratory and is considered to be clinically useful. Finally, there are other tests that can be performed on BALfluid on a case-by-case basis and may be helpful in specific clinical circumstances. Analysis by a cytopathologist is indicated if there are isolated cells that are suspicious for malignancy. Periodic Acid Schiff staining or Oil Red O staining may be helpful if pulmonary alveolar proteinosis or aspiration is suspected, respectively. Hemosiderin staining may be performed if hemorrhage is suspected and/or the initial BAL raises the suspicion of hemosiderin-laden macrophages.

5. RESULTS

Statistical Analysis Plan

Cellular analysis will be separately compared between different types of ILDs using the Mann–Whitney U test. Associations between phenotypic characteristics will be studied by Pearsons coefficient of correlation. All analyses will be performed with SPSS version 14.0 (SPSS Inc., Chicago, IL) and $p<0.05$ was considered significant.

6. APPENDIX

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INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE,CHENNAI-3

EC Reg No.ECR/270/Inst./TN/2013
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CERTIFICATE OF APPROVAL

To
Dr.C Ammaiyappan Palaniswamy,
PG in Thoracic Medicine,
Institute of Thoracic Medicine,
Madras Medical College,Chennai-3

Dear Dr. C.Ammaiyappan,

The Institutional Ethics Committee of Madras Medical College, received and discussed your application for approval of the proposal entitled "Broncholveolar lavage (BAL)cellular Analyses as Diagnostics Intervention for patients with suspected ILD in Conjuction with HRCT Imaging" s" No 33032014

The following members of Ethics Committee were present in the meeting held on 11.03.2014 conducted at Madras Medical College -3

1. Dr. C Rajendran ,M.D	-- Chairperson
2. Dr. R Vimala ,M.D. Dean ,MMC,Ch-3	-- Deputy Chairperson
3. Prof.Kalaiselvi,M.D Vice Principal,MMC,Ch-3	-- Member Secretary
4. Prof .Nandhini ,M.D, Inst .of Pharmacology ,MMC,Ch-3	-- Member
5. Prof. Bhavani Shankar,M.S, Prof &HOD	-- Member
6. Prof.V.Padmavathi,M.D, I/C Director of Pathology,MMC,Ch-3	-- Member
7. Thiru S.Govindasamy,BABL,	-- Lawyer
8. Tmt. Arnold Saulina,MA,MSW	-- Social Scientist
9. Thiru.S.Ramesh Kumar, Administrative Officer,MMC,Ch-3	-- Lay Person

We approve the proposal to be concucted in its presented form

Sd/Chairman&OtherMember

The institutional Ethics Committee expects to be informed about the progress of the Study ,and SAEoccuring in the course of the study ,any changes in the protocol and Patients information/ informed consont and asks to be provided a copy of the final report.

4/4/14

Member Secretary/Secretary,Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE

3/4/14

ஆராய்ச்சித் தகவல் தாள்

ஆராய்ச்சி தலைப்பு :

ILD நோய் (நுரையீரல் சுருங்கும் நோய்) உள்ளவர்களுக்கு மூச்சுக்குழாய் உள்நோக்கி கருவி மூலம் செய்யப்படும் கழுவல் நீரில் உள்ள உயிரணுக்கள் பரிசோதனை செய்தல் மூலம் நோயின் உட்பிரிவுகளை கண்டறிதல்.

முதன்மை ஆராய்ச்சியாளர் : மரு.C.அம்மையப்பன் பழனிசுவாமி

ஆராய்ச்சி வழிகாட்டுதல் : பேராசிரியர் மரு.D.ரங்கநாதன்

மரு.V.சுந்தர்

ஆராய்ச்சி செய்யப்படும் இடம் : இராஜீவ் காந்தி அரசு பொது மருத்துவமனை,

சென்னை.

தங்களை இந்த ஆராய்ச்சியில் பங்கேற்க அழைக்கின்றோம். இந்த தகவல் தாளில் இந்த ஆராய்ச்சியில் பங்கேற்பதற்கு தாங்கள் முடிவெடுப்பதற்கு உதவியான தகவல்களை குறிப்பிட்டுள்ளோம்.

ஆராய்ச்சியில் செய்யப்படும் பரிசோதனைகள் :

HRCT எனப்படும் கதிரியல் படத்தின் மூலம் தங்களுக்கு ILD நோய் கண்டறிந்த பிறகு, தங்களுக்கு

1. இரத்தப் பரிசோதனை
2. மூச்சுக் குழாய் உள்நோக்கி கருவி மூலம் செய்யப்படும் கழுவல் (Bronchoalveolar Lavage).

ஏற்படக் கூடிய ஆபத்து :

1. மூச்சுத் திணறல்
2. இரத்த கசிவு

ஏற்படக் கூடிய நன்மை :

நோய் வகையை துல்லியமாக கண்டறிதல் மூலம் அதற்கேற்ற சிகிச்சை முறை.

இந்த ஆராய்ச்சி மூலம் கண்டறியப்படும் தகவல்கள் மூலம் எதிர்காலத்தில் இந்நோய் பாதிக்கப்படுபவர்களுக்கு மருத்துவமுறைகளில் மற்றும் நோய் கண்டறிதலில் நன்மைகள் கிடைக்கலாம்.

இந்த ஆராய்ச்சி மருத்துவ பத்திரிக்கைகளில் பிரசுரிக்கப்பட்டாலோ, மருத்துவ மாநாடுகளில் விளக்கப்பட்டாலோ தங்களைப் பற்றிய அந்தரங்க தகவல்களை வெளியிடமாட்டோம்.

இந்த ஆராய்ச்சியில் தங்களுக்குப் பங்கேற்க விருப்பம் இல்லை என்றாலும் தங்களுக்கு உரித்தான மருத்துவ கவனிப்பு மற்றும் மருத்துவருடனான உறவு பாதிக்கப்படாது.

தாங்கள் இந்த ஆராய்ச்சியில் பங்குப்பெற சம்மதித்த பிறகு, மனம் மாறி தாங்கள் விலகிக் கொள்ள எந்த கட்டத்திலும் உங்களுக்கு உரிமை உள்ளது. அதற்குக் காரணம் ஏதும் கூற அவசியம் இல்லை.

ஆராய்ச்சியாளர் கையொப்பம் பங்கேற்பாளர் கையொப்பம்

இடம் :

தேதி :

INFORMATION TO PARTICIPANTS

Title :

Bronchoalveolar lavage cellular analyses as a Diagnostic Intervention for patients with suspected ILD in conjunction with HRCT imaging.

Principal investigator :

Dr. C AMMAIYAPPAN PALANISWAMY

Guide:

Prof. Dr. D. RANGANATHAN

Co-Guide:

Dr. V. SUNDAR

You are invited to take part in this study. The information in this document is meant to help you decide whether or not to take part. Please feel free to ask if you have any queries or concerns.

What is the purpose of this study?

Interstitial lung disease is a progressive disease of the lungs. To optimize the BAL- Bronchoalveolar lavage procedure as per recommendations put forth by the American Thoracic Society for the cellular analyses of Interstitial lung diseases, which aids to diagnose the subtypes of ILD.

Study design and procedures :

A prospective study, which involves the BAL procedure after obtaining fitness for the procedure from concerned specialists, and blood investigations, which involves prick with a needle and syringe, of about 15ml of blood.

Possible Risks:

The procedure has some risks of hemorrhage from the lavage site.

Possible benefits to you:

In helping diagnose the subtype of the ILD, which night help us tailor the treatment required / and in prognosis.

Possible benefits to other people:

The results of the study might provide benefits to the society in terms of advancement of medical knowledge and / or Therapeutic benefits to future patients.

Confidentiality of the information obtained from you:

You have the right to confidentiality regarding the privacy of your personal information. The information from this study if published or presented in scientific journals / meetings, your identity will not be revealed.

How will your decision in not to participate in the study affect you?

Your decision not to participate in this study will not affect your medical care or your relationship with the investigator or the institution.

You will not lose any benefits to which you are otherwise entitled.

Can you decide stop participating in the study once you have agreed?

The participation in this study is purely voluntary and you have the right to withdraw from this study at anytime during the course of this study without giving reasons.

Signature of the Investigator **Signature of the Participant**

Date :

Place:

ஒப்புதல் தாள்

எனக்கு நுரையீரல் சுருங்கும் நோய் உள்ளது என்பதையும், அதற்காக மூச்சுகுழாய் உள்நோக்கி கருவி மூலம் செய்யப்படும் கழுவல் நீரில் உள்ள உயிரணுக்கள் பரிசோதனை மற்றும் அதன் பலன்கள், பக்கவிளைவுகள் பற்றி தெரிந்து கொண்டேன் இப்பரிசோதனை செய்து கொள்ள சம்மதிக்கின்றேன்.

இப்படிக்கு

CONSENT FORM

I have been told about the bronchoalveolar lavage procedure and the possible side effects. I am willing to undergo this procedure.

S.NO			ID Number	MRD NO	AGE/GEN	OCCUPATION	C/O	DURATION	SMOK	EXPOSURE ALCO	ASBES OA	SILI	HON	ALE	TB	VIR	DISEASES AST	RA	SLE	SCL	PULSE	BP	ASE	JVP	OED	GENERAL EXAM LUBRING	CVS	ABD	CNS	JOINT	SKIN	CHEST EXAM R/K	EXF	ICM	PAL	BLOOD INV BS	WBE	CREP	RON	HB	TC	P	LY	E	MO	PLT	4TH	PFT	HRCT PATTERN
	1	1	IPF1		49/M	COCONUT GODOW	EXERTIONAL DYSPNOE	2YEARS	NIL	NIL	NIL	NIL	NIL	NIL							90/MIN	80/M	NO	NOT RAIS	NIL	PRESENT	NAD	NAD	NAD	NAD	NAD	20/MIN				NVBSNIL		BIBASILAR	NIL	11.4GM	6400	52%	30%	9%		2.95LAKHS	RESTRICTIVE P	UIP (?IHISTOLOG
	2	2	IPF2		54/M	CLERICAL STAFF I	EXERTIONAL DYSPNOE	2YEARS	YES	NIL											100/MI	120/80	"	"	"	"	"	"	"	"	20/MIN				"	"	"	"	13.4GM	6900	71%	26%	1%		3LAKHS/CM	"	UIP (?IHISTOLOG
	3	3	IPF4		52/M	GROCERY STORE	EXERTIONAL DYSPNOE	2YEARS	YES	NIL											94/MIN	120/70	NIL	"	"	"	"	"	"	"	26/MIN				"	"	"	"	14GM	###	51%	30%	###		3.75LAKHS	"	UIP (?IHISTOLOG
	4	4	IPF5		37/M	CLERICAL STAFF I	EXERTIONAL DYSPNOE	2YEARS	NO	NO											80/MIN	110/70	NIL	"	"	"	"	"	"	"	28/MIN				"	"	"	"	12.1GM	6100	52%	31%	4%	3%	2.4LAKHS	"	UIP (?IHISTOLOG
	5	5	IPF6		56/M	BUS DRIVER	EXERTIONAL DYSPNOE	2YEARS	YES	YES											104/MI	110/70	NIL	"	"	"	"	"	"	"	30/MIN				"	"	"	"	14.3GM	8300	58%	30%	2%		2.9LAKHSM	"	UIP (?IHISTOLOG
	6	6	IPF7		54/M	AGRICULTURAL LA	EXERTIONAL DYSPNOE	1YEAR	NO	YES											78/MIN	110/70	NIL	"	"	"	"	"	"	"	24/MIN				"	"	"	"	13.4GM	###	52%	40%	8%		4.2Lakhs	"	UIP (?IHISTOLOG
	7	7	IPF7		44/M	COTTON MILL	"	4YEARS	YES	YES											96/MIN	110/80	NIL	"	"	"	"	"	"	"	30/MIN				"	"	"	"	14.5GM	###	42%	51%	7%		4LAKHS	"	UIP (?IHISTOLOG
	8	8	LCH1		49/M	GOLDSMITH	DRY COUGH	6MONTHS	NO	NO											86/MIN	120/80	"	"	"	"	"	"	"	"	36/MIN				"	"	FINE INSP-R"		15.9GM	DL	63%	25%	###		3.6LAKHS	"	UIP (?IHISTOLOG
			HYPERSENSITIVITY PNEUMONITIS																																											
	9	1	HP1		75/M	AGRICULTURAL LA	EXERTIONAL DYSPNOE	20YEARS	NO	YES	PESTICIDES										76/MIN	140/80	NO	NOT RAIS	NIL	PRESENT	NAD	NAD	NAD	NAD	NAD	24/MIN				NVBSOCC.WHEEZE		B/L UPPER	OCCAS	8.8GM	###	54%	40%	6%		3.75LAKHS	RESTRICTIVE	
	10	2	HP2		54/M	CONSTRUCTION LA	EXERTIONAL DYSPNOE	10YEARS	YES	YES											80/MIN	140/70	"	"	"	"	"	"	"	"	22/MIN				NVBSPRESENT		FINE CREPS	PRES	13.8GM	6400	63%	24%	3%		4.2LAKHS	RESTRICTIVE	
	11	3	HP3		61/F	COTTON MILL	EXERTIONAL DYSPNOE	15YEARS	NO	NO	COTTON DUST										88/MIN	100/60	"	"	"	"	"	"	"	"	26/MIN				"	"		PRES	10.7GM	8400	68%	18%	###	2%	3.75LAKhs	RESTRICTIVE	
	12	4	HP4		55/M	TEACHER	EXERTIONAL DYSPNOE	10YEARS	NO	NO		PRESENT									72/MIN	140/80	"	"	"	"	"	"	"	"	24/MIN				"	"	"	"	13.2GM	8200	63%	30%	8%	1%	2.95LAKHS	RESTRICTIVE	
	13	5	HP5		65/M	PRINTING INDUSTR	EXERTIONAL DYSPNOE	40YEARS	YES	YES											80/MIN	130/70	"	"	"	"	"	"	"	"	28/MIN				NVBS*		"	"	11.5GM	8400	55%	4%			3.4LAKHS	RESTRICTIVE	
	14	6	HP6		37/M	PLASTIC INDUSTRY	EXERTIONAL DYSPNOE	10YEARS	NO	YES											76/MIN	130/90	NIL	"	"	"	"	"	"	"	24/MIN				"	"	"	"	13.2GM	8600	60%	30%	6%		2.6Lakhs/mmRESTRICTIVE		
	15	7	HP7		58/M	POULTRY FARMIN	EXERTIONAL DYSPNOE	15YEARS	NO	YES											88/MIN	120/70NMHG	"	"	"	"	"	"	"	"	26/MIN				"	"	"	"	12.8GM	7067	54%	30%	7%		3.75LAKHS	RESTRICTIVE	
	16	8	HP8		25/F	POULTRY FARMIN	COUGH,DYSPNOEA	ACU 14DAYS	NO	NO											96/MIN	130/70	NO	"	"	NIL	"	"	"	"	28/MIN				"	PRESENT	PRESENT	PRES	9.4GM	18800	35%	80%	###		2.8Lakhs	MIXED	
	17	9	HP9		58/m	AGRICULTURAL LA	EXERTIONAL DYSPNOE	40years	no	no		PESTICIDES									76/MIN	130/80	NO	"	"	PRESENT	"	"	"	"	22/MIN				"	NIL	PRESENT		10.8GM	5500	55%	40%	5%		1.8LAKHS	RESTRICTIVE	
	18	10	HP10		58/F	RICEMILL	EXERTIONAL DYSPNOE	10YEARS	NO	NO											80/MIN	120/70	NO	"	"	"	"	"	"	"	28/MIN				"	PRESENT	PRESENT	PRES	9.8GM	10500	56%	40%	2%		2.5LAKHS	RESTRICTIVE	
	19	11	HP11		26/M	RICEMILL	COUGH,DYSPNOEA	ACU 20DAYS	NO	NO											96/MIN	110/80	NO	NOT RAIS	NIL	NIL	"	"	"	"	24/MIN				"	"	"	"	13.2GM	8700	65%	34%	4%		3.8LAKHS	MIXED	
	20	12	HP12		58/M	AGRICULTURAL LA	EXERTIONAL DYSPNOE	10YEARS	NO	NO		PESTICIDES									76/MIN	140/90	NO	NOT RAIS	NIL	PRESENT	NAD	NAD	NAD	NAD	NAD	25/MIN				"	"	"	"	12.4GM	8400	61%	32%	7%		3.2LAKHS	RESTRICTIVE	
	21	13	HP13		72/M	AGRICULTURAL LA	EXERTIONAL DYSPNOE	20YEARS	NO	YES		PESTICIDES									80/MIN	120/70	NO	"	"	PRESENT	NAD	NAD	NAD	NAD	NAD	22/MIN				NVBSNIL		PRESENT	NIL	11.8GM	8000	52%	44%	4%		1.8LAKHS	RESTRICTIVE	
	22	14	HP14		46/M	PHARMACEUTICAL	EXERTIONAL DYSPNOE	10YEARS	YES	NO											72/MIN	110/70	NO	"	"	PRESENT	NAD	NAD	NAD	NAD	NAD	20/MIN				"	NIL	PRESENT	NIL	13.8GM	9100	58%	37%	5%		2.5LAKHS	MIXED	
			CONNECTIVE TISSUE DISORDERS																																											
	23	1	CVD1		45/F	HOMEMAKER	EXERTIONAL DYSPNOE	1YEAR	NO	NO	NIL	NIL	NIL	NIL	NIL	NIL	NIL		7RHEUMATO	YES	80/MIN	110/80	NIL	NOT RAIS	NIL	PRESENT	NAD	NAD	NAD	NAD	NAD	F/O CU	24/MIN				NVBS		BIBASILAR	NIL	9.8GM	###	54%	32%	###		2.9LAKHS/MRESTRICTIVE		
	24	2	CVD2		61/F	TEACHER	EXERTIONAL DYSPNOE	2YEARS	"	"	"	"	"	"	"	"	"		YES.ON TREATMENT		88/MIN	110/70	FREQE	"	"	PRESENT	NAD	NAD	NAD	NAD	NAD	F/O RHEU NAD	26/MIN				NVBS		BIBASILAR CREP		8.9GM	###	65%	20%	###	3%	2.95LAKHS	RESTRICTIVE	
	25	3	CVD3		58/M	CLERICAL STAFF	EXERTIONAL DYSPNOE	2YEARS	NO	"	"	"	"	"	"	"	"		YES.ON TREATMENT		80/MIN	110/80	NIL	"	"	PRESENT	NAD	NAD	NAD	NAD	NAD	F/O RHEU FOALO	28/MIN				NVBS		BIBASILAR CREP		13.9GM	11400	80%	14%	6%		3.45LAKHS	RESTRICTIVE	
	26	4	CVD4		53/F	HOME MAKER	EXERTIONAL DYSPNOE	5YEAR	"	"	"	"	"	"	"	"	"		RHEUMATOID ON TR		94/MIN	120/80	"	"	"	PRESENT	NAD	NAD	NAD	NAD	NAD	F/O RHEU ATOID	25/MIN				NVBS		B/L CREPS		9.8GM	###	80%	10%	2%		2.9LAKHS/MRESTRICTIVE		NSIP PATTERN
	27	5	CVD5		64/F	HOME MAKER	EXERTIONAL DYSPNOE	1YEAR	"	"	"	"	"	"	"	"	"		RHEUMATOID ON TR		92/MIN	130/80	"	"	"	PRESENT	NAD	NAD	NAD	NAD	NAD	F/O RHEUMATOID	30/MIN				NVBS		B/L CREPS		11.2GM	8200	61%	35%	4%		3.4LAKHS	RESTRICTIVE	NSIP PATTERN
	28	6	CVD6		44/M	BUS DRIVER	EXERTIONAL DYSPNOE	1YEARS	YES	YES	"	"	"	"	"	"	"		RHEUMATOID ON TR		80/MIN	110/70	NIL	"	"	"	NAD	NAD	NAD	NAD	NAD	F/O RHEUMATOID	28/MIN				NVBS		BIBASILAR CREP		8.6GM	10200	55%	42%	###		2.4LAKHS/MRESTRICTIVE		NSIP PATTERN
	29	7	CVD7		22/F	CLERICAL STAFF	NO RESPIRATORY SYMPTOMS		NO	NO	"	"	"	"	"	"	"		SYSTEMIC SCLEROSI		78/MIN	110/70	NIL	"	"	"	NAD	NAD	NAD	NAD	NAD	F/O SYSTEMIC SC	30/MIN				NVBSNIL		NIL		9.2GM	10400	60%	37%	3%		3.2LAKHS	NORMAL	
	30	8	CVD8		26/F	HOME MAKER	NO RESPIRATORY SYMPTOMS		NO	NO	"	"	"	"	"	"	"		SYSTEMIC SCLEROSI		70/MIN	120/80NMHG	"	"	"	NIL	NAD	NAD	NAD	NAD	NAD	F/O SYSTEMIC SC	30/MIN				NVBS		BIBASILAR CREP		13GM	10900	75%	20%	5%		2.7LAKHS	NORMAL	UIP
			SARCOIDOSIS																																										
	31	1	SAR1		35/F	HOME MAKER	MILD EXERTIONAL DYSPNOEA		NO	NO	"	"	"	"	"	"	"				80/MIN	120/80	NIL	NIL	NIL	NIL	NAD	NAD	NAD				18/MIN				NVBS		NIL		9.8GM	6500	56%	42%	2%		3.8LAKHS	NORMAL	
	32	2	SAR2		42/F	HOME MAKER	NO RESPIRATORY SYMPTOMS		NO	NO	"	"	"	"	"	"	"		AXILLARY LYMPHNO		84/MIN	120/70	NIL	NIL	NIL	NIL	NAD	NAD	NAD				19/MIN				NVBS		NIL		10.8GM	5600	60%	38%	2%		1.8LAKHS	NORMAL	
	33	3	SAR3		45/F	HOME MAKER	EXERTIONAL DYSPNOEA		NO	NO	"	"	"	"	"	"	"		ERYTHEMA N		80/MIN	110/70	NIL	NIL	NIL	NIL	NAD	NAD	NAD			ERYTHEMA NO	DDS	6/MIN				NVBS		CREPS+		8.9GM	###	70%	28%	2%		2.7LAKHS	RESTRICTIVE	
			PNEUMOCONIOSES																																										
	34	1	SIL1		41/M	DENTAL PROSTHET	EXERTIONAL DYSPNOEA		YES	YES	"	"	CERA'								116/MI	110/70		RAISED	FRESE	PRESENT	NAD	NAD	NAD				16/MIN				NVBSPRESENT		CREPS+		10.8GM	8700	48%	40%	###		1.8LAKHS	MIXED	
	35	2	SIL2		54/M	GRANITE QUARRY	EXERTIONAL DYSPNOEA		YES	YES			SILICA DUST								90/MIN	130/70		RAISED	FRESE	PRESENT	NAD	NAD	NAD				18/MIN				NVBSPRESENT		CREPS+		14.3GM	8300	60%	20%	###		2.3LAKHS	MIXED	
	36	3	SIL3		49/M	SANDBLASTING	EXERTIONAL DYSPNOEA		NO	NO			SILICA DUST								86/MIN	130/80		RAISED	FRESE	PRESENT	NAD	NAD	NAD				22/MIN				NVBSPRESENT		CREPS+		14.8GM	8200	30%	56%	6%		1.95LAKHS	MIXED	
	37	4	SIL4		39/M	SANDBLASTING	EXERTIONAL DYSPNOEA		YES	YES			SILICA DUST								114/MI	100/70		RAISED	FRESE	PRESENT	NAD	NAD	NAD				26/MIN				NVBSPRESENT		PRESENT		13.2GM	8300	45%	50%	5%		2.8LAKHS	MIXED	
	38	5	SIL5		51/M	SANDBLASTING	EXERTIONAL DYSPNOEA		YES	NO			SILICA DUST								98/MIN	140/90		NOT RAIS	NIL	PRESENT	NAD	NAD	NAD				30/MIN				NVBSPRESENT		CREPS+		13.4GM	8800	61%	34%	5%		2.9LAKHS	MIXED	
			ARDS																																										
	39	1	ARDS1		60/F	HOME MAKER	REFRACTORY HYPOXEMIA,ON VENNO		NO												112/MI	120/70		NOT RAIS	NIL	NIL	NAD	POST-LAPAROTOMY			16/MIN				NVBSPRESENT		PRESENT		8.7GM	19200	82%	10%	8%		1.9LAKHS	NOT DONE		CXR;B/L PATCHY
	40	2	ARDS2		44/M	AGRICULTURAL LA	REFRACTORY HYPOXEMIA,ON VENYES			YES											100/MI	110/68		NOT RAIS	NIL	NIL	NAD				12/MIN				NVBSPRESENT		PRESENT		13.8GM	8500	64%	12%	4%		2.4LAKHS	NOT DONE		CXR;B/L PATCHY
			Eosinophilic lung diseases																																										
	41	1	ELD1		35/F	AGRICULTURAL LA	WHEEZE,PERSISTENT,R	2YEARS	NO	NO											90/MIN	120/80		NR	NIL	PRESENT	NAD				22/MIN				NVBSWHEEZE				12.4GM	###	48	37	15		3.8LAKHS	OBSTRUCTIVE		HRCT;PROXIMA BRONCHIECTAS OF RIGHT ULML LEFT LL MUCOID IMPAC
	42	2	ELD2		46/F	home maker	wheeze	6years	NO	NO											80/MIN	110/70		NOT RAIS	NIL	PRESENT	NAD	NAD	NAD	NAD	NAD	28/MIN				NVBSWHEEZE		PRESENT		12.4	###	38%	50	12		2.9LAKHS	OBSTRUCTIVE		PROXIMAL BRO B/L UPPER LOBE RIGHT MIDDLE
			LYMPHANGITIC CARCINOMATOSA																																										
	43	1	LC1		65/F	HOME MAKER	DYSPNOEA	1MONTH	NO	NO											POST MASTECTOMY FOR CA.BREAST, FOLLOWED BY CHEMORADIAT				92/MIN	100/60	MMHG	NR		NIL	NIL	NAD	NAD	NAD	NAD	NAD	22/MIN				NVBSNIL		NIL		8.9	###	40%	50%	5%		1.8LAKHS	RESTRICTIVE		INTERLOBAR FI B/L PLEURAL EF INTERLOBULAR
	44	2	LC2		61/F	HOME MAKER	DYSPNOEA	2MLONTHS	NO	NO											POST MASTECTOMY CA.BREAST FOLLOWED BY CHEMORADIATION-2011				76	110/80		NR		NIL	NIL	NAD	NAD	NAD	NAD	NAD	18/MIN				NVBSNIL		YES		11.3GM	###	60%	38%	2%		2.4LAKHS	RESTRICTIVE		SAME AS ABOVE
			ASPIRATION BRONCHIOLITIS																																										
	45	1	AB		20/F	HOME MAKER	DYSPNOEA,COUGH	2YEARS	NO	NO											KNOWN PSYCHIATRIC ILLNESS ON ANTO ANTI-PSYCHOTIC MEDICATIONS FOR 4YEARS				90/MIN	110/70		NR		NIL	NIL	NAD	NAD	NAD	NAD	NAD	22/MIN				NVBSNIL		CREPS+		10.4GM	###	63%	35%	2%		1.8L		mixed pattern	B/L centrilobular upper lobe mixed right sixth segmen b/l postcrebaal an
			IPF																																										
	46	8	IPF8		50/f	home maker	exertional dyspnoea	4years	no	no											96	120/70		nr	nil	grade3 clubbing						28/min				nvbs		crepe+velcro		8.7gm	11000	eu(leucos)	65%	30%	5%	2.7lakhs	restrictive		b/l subpleural/base extensive honeycon sparing of upper lo
	47	15	HP15		55/m	baker	exertional dyspnoea	5years	no	no	biomass fuel exposure										88/min	130/80		nr	nil	grade2	nad	nad	nad	nad	nad	24/min				nvbs		crepsdine		13.8gm	###	63	34	3%		2.8		mixed	b/l upper lobe, lingular fibrosis, basal reticulations
			connective tissue/CVD-ILD																																										
	48	9	CVD9		48/f	home maker	exertional dyspnoea	9m/year	no	no									features of rheumatoid arthritis+		78/min	120/70		NR	nil	grade2	nad	nad	nad		f/o rheumatoid		22/min				nvbs		creps		11gm%	###	84	32	4		2.3		restrictive	b/l ground glass op subpleural/basal traction bronchier
			hypersensitivity pneumonitis																																										
	49	16	HP16		60/m	agricultural laborer	exertional dyspnoea	6years	no	yes	pesticides, hay dust										90/min	130/80		nr	nil	gr2	nad	nad	nad				24/min				nvbs		creps		12gm%	###	64%	36%	###		2.1lakhs		mixed	b/l fibrosis-upper l subpleural/basal re mild honeycombi
	50	17	HP17		38/m	arc welder	exertional dyspnoea	3 years	no	yes	welding fumes metal dust										88	120/80		nr	nil	grade2	nad	nad	nad				22/min				nvbs		creps		13.8gm	###	70%	26%	4%		2.9lakhs		mixed	b/l upper lobe fibr subpleural/basal re

HRCT	TCC	RES	BAL AM	MC	LY	NE	EOS	INTROCYTES	OTH	PROVISIONAL DIAGNOSES	FINAL DIAGNOSIS	SITE OF BAL	CYTOLOGY	CORRECTIVE DIAGNOSIS
SUB-PLEURAL/BASAL RETICULATIONS AND HONEY	85CELLS/MM3		35%		###	52%				IIDIOPATHIC PULMONARY FIBROSIS-ACUTE EXACERBATION		RIGHT LOWER LOBESYM	ACUTE INFLAMMATORY	ACUTE IIDIOPATHIC PULMONARY FIBROSIS WITH ? SUPERADDE
"	90CELLS/MM3		46%		###	34%			600	"	"	RIGHT LOWER LOBE	"	
"	80CELLS/MM3		35%		###	24%	6%					RIGHT LOWER LOBE	"	
"	80CELLS/MM3		60%		###	35%				IIDIOPATHIC PULMONARY FIBROSIS_STABLE	IPF-STABLE	RIGHT LOWER LOBE	INFLAMMATORY SMEAR	
"	90CELLS/75MM3		35%		###	38%	2%			IPF-ACUTE EXACERBATION	IPF-AE	"	ACUTE INFLAMMATORY	
"	78cells/mm3		60%		###	12%				IPF	IPF	RIGHT MIDDLE LOBE		
"	800CELLS/MM		50% 20%	10%	5%	5%			10%	IPF	IPF-STABLE	RIGHT MIDDLE LOBE	ACUTE INFLAMMATORY PATHOL	
" AND TRACTION BRONCHIECTASIS	100CELLS/MM3				###			90%		IPF	IPF	RIGHT LOWER LOBE	NO EVI MALIGNANCY/TUBERCULOSIS	
B/L UPPER LOBE FIBROSIS,TRACTION BRONCHIECT	80CELLS/MM3		45%		###	5%				CHRONIC HYPERSENSITIVITY PNEUMONITIS	CHR.HYPERSENSITIVITY PNEUM	RIGHT UPPER LOBE	INFLAMMATORY SMEAR	
B/L UL FIBROSIS	60CELLS/MM3		45%		###	20%	3%			CHRONIC HYPERSENSITIVITY PNEUMONITIS	CHR.HYPERSENSITIVITY PNEUM	RIGHT UPPER LOBE	INFLAMMATORY SMEAR	
b/l fibrosis with sparing of bases. Centrilobular nodules	100cells/mm3	8%	4%		4%	84%				CHR.HP WITH ACUTE EXACERBATION	CHR.HP WITH ACUTE EXACERB	RIGHT UPPER LOBE	ACUTE INFL.PATHOLOGY	
GROUND GLASS OPACITIES,B/L UPPER LOBE FIBROSI	60CELLS/MM3		51%		###	8%				CHRONIC HYPERSENSITIVITY PNEUMONITIS	CHRONIC HYPERSENSITIVITY P	RIGHT UPPER LOBE	INFLAMMATORY SMEAR	
B/L UL FIBROSIS	120CELLS/MM3		60%		###	5%				CHRONIC HYPERSENSITIVITY PNEUMONITIS	CHRONIC HYPERSENSITIVITY P	LEFT UPPER LOBE	CHRONIC INFLAMMATORY SMEAR	
B/L UL FIBROSIS WITH CENTRILOBULAR NODULES	90CELLS/MM3		45%		###	10%				CHRONIC HYPERSENSITIVITY PNEUMONITIS	CHRONIC HYPERSENSITIVITY P	RIGHT UPPER LOBE	INFLAMMATORY SMEAR	
B/L UPPER LOBE AND LINGULAR FIBROSIS	85CELLS/MM3		50%		###	8%				CHRONIC HYPERSENSITIVITY PNEUMONITIS	CHRONIC HYPERSENSITIVITY P	LINGULA	INFLAMMATORY SMEAR	
b/l ground glass opacities,centrilobularAM nodules,air trappin	85CELLS/MM3		37%		###	8%				ACUTE HYPERSENSITIVITY PNEUMONITIS		RIGHT MIDDLE LOBE	INFLAMMATORY SMEAR	
B/L UPPER LOBE FIBROSIS,BASAL RETICULATIONS	95CELLS/MM3		50%		###	5%				CHRONIC HYPERSENSITIVITY PNEUMONITIS	CHRONIC HYPERSENSITIVITY P	RIGHT UPPER LOBE	INFLAMMATORY SMEAR	
B/L UL FIBROSIS,CENTRILOBULAR NODULES	80CELLS/MM3		45%		###	15%				CHRONIC HYPERSENSITIVITY PNEUMONITIS	CHRONIC HYPERSENSITIVITY P	RIGHT UPPER LOBE	INFLAMMATORY SMEAR	
b/l ground glass opacities,centrilobularAM nodules,air trappin	110CELLS/MM3		30%		###	12%				ACUTE HYPERSENSITIVITY PNEUMONITIS	ACUTE HYPERSENSITIVITY PNE	RIGHT MIDDLE LOBE	ACUTE INFL.PATHOLOGY	
B/L UL FIBROSIS,BASAL RETICULATIONS	90CELLS/MM3		40%		###	14%				CHRONIC HYPERSENSITIVITY PNEUMONITIS	CHRONIC HYPERSENSITIVITY P	RIGHT LOWER LOBE	INFLAMMATORY SMEAR	
B/L UL FIBROSIS,BASAL HONEYCOMBING	80CELLS/MM3		60%		###	10%				CHRONIC HYPERSENSITIVITY PNEUMONITIS	CHRONIC HYPERSENSITIVITY P	RIGHT LOWER LOBE	INFLAMMATORY SMEAR	
B/L UL FIBROSIS,BASAL HONEYCOMBING	78CELLS/MM3		51%		###	11%				CHRONIC HYPERSENSITIVITY PNEUMONITIS	CHRONIC HYPERSENSITIVITY P	RIGHT LOWER LOBE	INFLAMMATORY SMEAR	
B/L BASAL INTRALOBULAR INTERLOBULAR SEPTAL 1	65CELLS/MM3		20%		###	10%				SCLERODERMA,?RHEUMATOID ,ILD	SCLERODERMA,?RHEUMATOID	RIGHT LOWER LOBE	INFLAMMATORY SMEAR	
PATCHY NODULAR OPACITIES,BASAL RETICULATIO	90CELLS/MM3		55%		###	40%				RHEUMATOID ARTHRITIS,ILD	RHEUMATOID ARTHRITIS,ILD	RIGHT LOWER LOBE	INFLAMMATORY SMEAR	
B/L UL,R7 ML,LT LL GROUND GLASS OPACITIES	85CELLS		60%		###	15%				RHEUMATOID ARTHRITIS,ILD	SJOGRTN'S,RHEUMATOID ARTH	RIGHT MIDDLE LOBE	INFLAMMATORY SMEAR	
B/L SYMMETRICAL GROUND GLASS OPACITIES	90CELLS/MM3		62%		###	10%				RHEUMATOID ARTHRITIS,ILD	RHEUMATOID ARTHRITIS,ILD	RIGHT MIDDLE LOBE		
B/L SYMMETRICAL GROUND GLASS OPACITIES	94CELLS/MM3		60%		###	8%				RHEUMATOID ARTHRITIS,ILD	RHEUMATOID ARTHRITIS,ILD	RIGHT LOWER LOBE	INFLAMMATORY SMEAR	
B/L SYMMETRICAL GROUND GLASS OPACITIES	94CELLS/MM3		54%		###	14%				RHEUMATOID ARTHRITIS,ILD	RHEUMATOID ARTHRITIS,ILD	RIGHT MIDDLE LOBE	INFLAMMATORY SMEAR	
BASALSUBPLEURAL RETICULATION	110CELLS/MM3		45%		###	20%				SYSTEMIC SCLEROSIS,EARLY ILD	SYSTEMIC SCLEROSIS,EARLY	RIGHT LOWER LOBE	INFLAMMATORY SMEAR ;	
B/L BASAL HONEYCOOMBING			73%		8%	20%				SYSTEMIC SCLEROSIS,EARLY ILD	SYSTEMIC SCLEROSIS,EARLY IL	RIGHT LOWER LOBE		
											"		CHRONIC INFL. PATHOLOGY	
RIGHT PARATRACHEAL,B/L HILAR ADENOPATHY,RI	90		20%		###	45%				SARCOIDOSIS	SARCOIDOSIS	RIGHT UPPER LOBE	ACUTE INFLAMMATORY PATHOLOGY	
RIGHT PARATRACHEAL,B/L HILAR ADENOPATHY,RI	100CELLS		40%		###	10%				SARCOIDOSIS	SARCOIDOSIS	RIGHT MIDDLE LOBE	INFLAMMATORY PATHOLOGY	
RIGHT PARATRACHEAL,RIGHT HILAR LYMPHADENO	140CELLS		60%		###	12%				SARCOIDOSIS	SARCOIDOSIS STAGE2	RIGHT MIDDLE LOBE	INFLAMMATORY PATHOLOGY	
CENTRILOBULAR NODULES,SUBPLEURAL NODULES	120CELLS/MM3		80%		###	5%				SILICOSIS,PROGRESSIVE MASSIVE FIBROSIS	SILICOSIS,PROGRESSIVE MASSI	RIGHT UPPER LOBE	CHRONIINFLAMMATORY PATHOLOGY	
B/L UPPER LOBE CENTRILOBULAR NODULES,HILAR	80CELLS/MM3		65%		###	10%				SILICOSIS	SILICOSIS	RIGHT UPPER LOBE	INFLAMMATORY SMEAR	
CONGLOMERATE NODULES B/L UPPER/LOWER LOB	140		60%		###	15%				SILICOSIS,PROGRESSIVE MASSIVE FIBROSIS	SILICOSIS,PROGRESSIVE MASSI	RIGHT UPPER LOBE	CHRONIINFLAMMATORY PATHOLOGY	
CONGLOMERATE NODULES B/L UPPER/LOWER LOB	90CELLS/MM#		72%		###	8%				SILICOSIS,PROGRESSIVE MASSIVE FIBROSIS	SILICOSIS,PROGRESSIVE MASSI	RIGHT UPPER LOBE	CHRONIINFLAMMATORY PATHOLOGY	
B/LUPPER LOBE FIBROSIS,CALCIFIED HILAR NODES	85CELLS		70%		###	6%				SILICOSIS	SILICOSIS	LEFT UPPER LOBE	INFLAMMATORY SMEAR	
V INFILTRATES MORE IN THE LOWER ZONES	340CELLS		30%		###	35%				ARDS,SECONDARY TO SEPSIS,COMPLICATION OF ILEAL PERFORATION		RIGHT MIDDLE LOBE	ACUTE INFLAMMATORY SMEAR	
Y INFILTRATES MORE IN THE LOWER ZONES	400	6%	HEMOSIDE		###	40%				ACUTE INFLAMMATORY PATHOLOGY		RIGHT MIDDLE LOBE		
L IS	160CELLS/MM3		52%		###	5%	20%			ABPA	ABPA	RIGHT MIDDLE LOBE	ACUTE INFLAMMATORY SMEAR	
TION>														
NCHIECTASIS	90CELLS/MM3		44%		###	8%	30%			ABPA	ABPA	RIGHT MIDDLE LOBE		
LOBE														
SSURE THICKENING FUSION SEPTAL THICKENING	100CELLS/MM3		60%		###	12%				LYMPHANGITIS CARCINOMATOSA	LYMPHANGITIC CARCINOMATO	RIGHT MIDDLE LOBE	CYTOLOGY POSITIVE FOR MALIGNANT CELLS	
	100CELLS/MM#		50%		###	20%				LYMPHANGITIC CARCINOMATOSA	LYMPHANGITIC CARCINOMATO	RIGHT MIDDLE LOBE	CYTOLOGY POSITIVE FOR MALIGNANT CELLS	
opacities segments s, egments with loss in bod appearance	96		54%		12	32				aspiration bronchiolitis	aspiration bronchiolitis	right upper lobe	inflammatory	
f reticulations ombing of basal segments bes	100cells/mm3		60%		###	12%				IPF exacerbation	IPF-exacerbation	right lower lobe basal segments	inflammatory	
	120cells	2%	64%		###	6%				chronic hypersensitivity pneumonitis	chronic hypersensitivity pneumonit	lingula	inflammatory	
acities basis	100		64%		###	12%				rheumatoid arthritis related ILD	rheumatoid arthritis related ILD	right lower lobe posterobasal	inflammatory	
ches ticulations ng	100		60		###	10				chronic hypersensitivity pneumonitis	chronic hypersensitivity pneumonit	right upper lobe		
asis ticulations	140		58%		###	15%				chronic hypersensitivity pneumonitis	chronic hypersensitivity pneumonit	right upper lobe	inflammatory	

S.NO	PATIENT	BAL D/D (Primary level)	BAL D/D (secondary level)	PFT D/D	HRCT D/D	CLINICAL + BALL	CLINICAL + HRCT +BAL	PROVISIONAL DIAGNOSIS
1	RADHAKRISHNAN	LYMPHOCYTE >15% (DD4) Sarcoidosis Nonspecific interstitial pneumonia (NSIP) Hypersensitivity pneumonitis Drug-induced pneumonitis Collagen vascular diseases Radiation pneumonitis Cryptogenic organizing pneumonia (COP) Lymphoproliferative disorders NEUTROPHILS >3% (DD2) Collagen vascular diseases Idiopathic pulmonary fibrosis Aspiration pneumonia Infection: bacterial, fungal Bronchitis Asbestosis Acute respiratory distress syndrome (ARDS) Diffuse alveolar damage (DAD)	D1, D2 LYMPHOCYTES >25% (DD4) Sarcoidosis Hypersensitivity pneumonitis NEUTROPHILS >50% (DD6) Acute lung disease Aspiration Pneumonia Suppurative infection	D1, D2	IPF ASBESTOSIS Chronic hypersensitivity pneumonitis Sarcoidosis CVD	Idiopathic pulmonary fibrosis Nonspecific interstitial pneumonia (NSIP) Acute lung disease Suppurative infection	Idiopathic pulmonary fibrosis Acute lung disease Suppurative infection	Acute Exacerbation of Idiopathic Pulmonary Fibrosis with superadded Infection
2	SIBVAKUMAR	DD1, DD2	D1, D2, D4	Restrictive pattern	same as above	Idiopathic pulmonary Fibrosis	Idiopathic pulmonary Fibrosis	Idiopathic pulmonary Fibrosis
3	JAWAHAR	DD1, DD2, EOSINOPHILS (>1%)(DD3) Eosinophilic pneumonias Drug-induced pneumonitis Zone sarcoid transplant Asthma, bronchitis Churg-Strauss syndrome Allergic bronchopulmonary aspergillosis Bacterial, fungal, helminthic, Pneumocystis infection Hodgkin's disease	D1, D2, D3, D4	Restrictive pattern	same as above	Idiopathic pulmonary Fibrosis Eosinophilic pneumonias Asthma, bronchitis Allergic bronchopulmonary aspergillosis Bacterial, fungal, helminthic, Pneumocystis infection	Idiopathic pulmonary Fibrosis Asthma, bronchitis Bacterial, fungal, helminthic, Pneumocystis infection	Acute Exacerbation of Idiopathic Fibrosis associated with Bronchitis/Asthma with superadded infection
4	SHANKAR	DD1, DD2	D1, D2, D4	Restrictive pattern	same as above	IPF hypersensitivity pneumonitis	Idiopathic pulmonary Fibrosis	Idiopathic Pulmonary Fibrosis
5	KAMARAJ	D1, D2, D3	D1, D2, D3, D4	Restrictive pattern	same as above	Idiopathic pulmonary Fibrosis Eosinophilic pneumonias Asthma, bronchitis Allergic bronchopulmonary aspergillosis Bacterial, fungal, helminthic, Pneumocystis infection	Asthma, bronchitis Bacterial, fungal, helminthic, Pneumocystis infection	Acute Idiopathic Fibrosis associated with Bronchitis/Asthma with superadded infection
6	SUBRAMANIAM	D1, D2	D1, D2	Restrictive pattern	same as above	Idiopathic pulmonary Fibrosis	Idiopathic pulmonary Fibrosis	Idiopathic Pulmonary Fibrosis
7	PRAKASH	UPPER AIRWAY CONTAMINATION	UPPER AIRWAY CONTAMINATION	Restrictive pattern	same as above	UPPER AIRWAY CONTAMINATION	Idiopathic pulmonary Fibrosis	Idiopathic Pulmonary Fibrosis
8	DAKSHINAMOORTI	LANGERHAN CELL HISTOCYTOSIS	LANGERHAN CELL HISTOCYTOSIS	Restrictive pattern	same as above	Pulmonary Langerhan cell Histocytosis	Idiopathic pulmonary Fibrosis Pulmonary Langerhan cell Histocytosis	Idiopathic pulmonary Fibrosis Pulmonary Langerhan cell Histocytosis
9	KASI	D1, D2	D4 LYMPHOCYTES >50% (D5) Hypersensitivity pneumonitis Nonspecific interstitial pneumonia (NSIP)	Restrictive pattern	dd fibrosis: hypersensitivity pneumonitis sarcoidosis silicosis reticrulerma associated ILD asbestosis	Hypersensitivity pneumonitis Nonspecific interstitial pneumonia (NSIP) Sarcoidosis Collagen vascular diseases Cryptogenic organizing pneumonia (COP) Lymphoproliferative disorders Idiopathic pulmonary fibrosis Aspiration pneumonia Infection: bacterial, fungal Bronchitis Asbestosis Acute respiratory distress syndrome (ARDS) Diffuse alveolar damage (DAD)	Hypersensitivity pneumonitis Bronchitis	Chronic Hypersensitivity Pneumonitis associated with Bronchitis
10	SAMBANDAM	D1, D2, D3	D4	Restrictive pattern	dd fibrosis	Hypersensitivity pneumonitis Sarcoidosis Nonspecific interstitial pneumonia (NSIP) Collagen vascular diseases Idiopathic pulmonary fibrosis Aspiration pneumonia Infection: bacterial, fungal Bronchitis Eosinophilic pneumonias Asthma, bronchitis Bacterial, fungal, helminthic, Pneumocystis infection	Hypersensitivity pneumonitis Nonspecific interstitial pneumonia (NSIP) Asthma, bronchitis Bacterial, fungal, helminthic, Pneumocystis infection	Acute Exacerbation of Hypersensitivity neumonitis with Bronchitis/Asthma
11	sagarathinam	D2	D2,D4	RESTRICTIVE PATTERN	dd fibrosis +dd centrilobular nodules endobronchial tb ABPA bronchiolitis	aspiration pneumonia suppurative infection ARDS bronchitis with infective exacerbation	chronic hypersensitivity pneumonitis with secondary infection	chronic hypersensitivity pneumonitis
12	Ashok	D1,D2	D1,D2,D4	restrictive pattern	dd fibrosis ggo dd:ARF,edema,hemorrhagic,infections-pcp Hypersensitivity pneumonitis Chr.eosinophilic pneumonia, bronchoalveolar cell carcinoma	chr.hypersensitivity pneumonitis ipf sarcoidosis lymphoid interstitial pneumonia	chronic hypersensitivity pneumonitis with infection	chronic hypersensitivity pneumonitis with secondary infective
13	Venkatesan	D1,D2	D1 D2 D4	restrictive pattern	dd fibrosis	hypersensitivity pneumonitis sarcoidosis ssip bronchitis	hypersensitivity pneumonitis more likely sarcoidosis	chronic hypersensitivity pneumonitis
14	Ramakrishnan	D1 D2	D1 D2 D4	restrictive lung disease	dd fibrosis dd centrilobular nodules	hypersensitivity pneumonitis sarcoidosis ssip-cellular	hypersensitivity pneumonitis	subacute hypersensitivity pneumonitis
15	rajaram	D1 D2	D1 D2 D4	restrictive	dd fibrosis	hypersensitivity pneumonitis bronchitis sarcoidosis IPF	hypersensitivity pneumonitis	
16	shankari	D1 D2	D1 D2 D5	restrictive	acute hypersensitivity pneumonitis dd ggo dd centrilobular nodules bronchiolitis obliterans	acute hypersensitivity pneumonitis	acute hypersensitivity pneumonitis	

17 Thangaraj	D1 D2	D1 D2 D4	restrictive	dd fibrosis	ipf hypersensitivity pneumonitis nsip	chronic hypersensitivity pneumonitis	
18 Murugammal	D1 D2	D1 D2 D4	restrictive		hypersensitivity pneumonitis IPF NSIP sarcoidosis infectious etiologies	hypersensitivity pneumonitis	
19 Rajesh	D1 D2	D1 D2 D5	restrictive	acute hypersensitivity pneumonitis dd ggo dd centrilobular nodules bronchitis obliterans	hypersensitivity pneumonitis NSIP Infectious Sarcoidosis	acute hypersensitivity pneumonitis	
20 kuppan	D1 D2	D1 D2 D4	restrictive	dd fibrosis	hypersensitivity pneumonitis NSIP Sarcoidosis Infectious bronchitis	chronic hypersensitivity pneumonitis	chronic hypersensitivity pneumonitis
21 vadhalingam	D1 D2	D1 D2 D4	restrictive	Chronic hypersensitivity pneumonitis IPF	Chronic hypersensitivity pneumonitis Sarcoidosis IPF Infective etiologies Bronchitis NSIP	chronic hypersensitivity pneumonitis	chronic hypersensitivity pneumonitis
22 Alagesan	D1 D2	D1 D2 D4	restrictive	Chronic hypersensitivity pneumonitis IPF	chronic hypersensitivity pneumonitis Sarcoidosis IPF NSIP INFECTIONs Bronchitis NSIP	Chronic hypersensitivity pneumonitis	chronic hypersensitivity pneumonitis
23 Elanjiyan	D1 D2	D1 D2 D5	restrictive	lymphangitis carcinomatosa pulmonary edema/hemorrhage IPF CVD	CVD IPF bronchitis hypersensitivity pneumonitis NSIP	CVD/CTD-ILD IPF	CTD ILD
24 Rajeswari	D1 D2	D1 D2 D4	restrictive	nip dd including IPF,CVD hypersensitivity pneumonitis NSIP LIP	ipf cvd sarcoidosis hypersensitivity pneumonitis	sarcoid hypersensitivity pneumonitis nsip ipf CVD bronchitis aspiration mbolysosis	CVD/CTD-ILD
25 Elsosabi	D1 D2	D1 D2	restrictive	dd ggo rheumatoid arthritis DIP AIP CVD	IPF,CVD,Bronchitis sclerosis Hypersensitivity pneumonitis,CVD	rheumatoid arthritis related ILD	rheumatoid arthritis ILD
26 tamilselvi	D1 D2	D1 D2 D4	restrictive	NSIP dd ggo	CVD IPF bronchitis, infections	rheumatoid arthritis related ILD	Rheumatoid arthritis related ILD
27 Kamala	D1 D2	D1 D2 D4	restrictive	CVD-dd NSIP dd ggo	CVD IPF Aspiration pneumonia ARDS Infection hypersensitivity pneumonitis sarcoidosis Lymphoproliferative disorders	rheumatoid arthritis related ILD	rheumatoid arthritis related ILD
28 Velumani	D1 D2	D1 D2 D4	restriction	DD ggo rheumatoid lung	IPF,CVD, aspiration,infection hypersensitivity pneumonitis,sarcoidosis lymphoproliferative disorders	Rheumatoid arthritis related ILD (CVD)	rheumatoid arthritis related ILD
29 Subathra	D1 D2	D1 D2	restrictive	IPF CVD	IPF CVD(CONNECTIVE TISSUE DISEASES) NSIP Sarcoidosis Hypersensitivity pneumonitis	systemic sclerosis with early ILD (CVD/CTD-ILD)	Systemic sclerosis with early ILD
30 Syed Rafyn Basu	D2	D2	restrictive	IPF Connective tissue disease hypersensitivity pneumonitis NSIP Drug fibrosis	IPF CVD Infections	Systemic sclerosis with early ILD(CTD-ILD)	
31 Mekraj Basu	D1 D2	D1 D2 D4	restrictive	sarcoidosis silicosis lymphoma lymphoproliferative disorders tuberculosis/fungal infections	CVD IPF Sarcoidosis Hypersensitivity pneumonitis Infections-TB/fungal	Sarcoidosis	Sarcoidosis
32 Bragadhan	D1 D2	D1 D2 D4	restrictive	same as above	same as above	Sarcoidosis, TB lymphadenopathy	Sarcoidosis(IIPE confirmed)
33 Kamatchi	D1 D2	D1 D2 D4	restrictive	same as above	same as above	sarcoidosis	sarcoidosis
34 Rajaiah	D2	D2	restrictive	silicosis sarcoidosis lymphangitis carcinomatosa hypersensitivity pneumonitis respiratory bronchiolitis bronchoalveolar carcinoma	CVD IPF bronchitis Infection	Silicosis	Silicosis
35 Annasamy	D1 D2	D1 D2 D4	restrictive	same as above	IPF,CVD,Infectious Sarcoid,Hypersensitivity pneumonitis NSIP Chronic beryllosis	Silicosis	Silicosis
36 Jani Basha	D1 D2	D1 D2 D4	restrictive	Silicosis with PMF pulmonary talc granulomatosis	IPF,CVD Infection,Bronchitis ARDS Sarcoidosis Silicosis NSIP,Hypersensitivity pneumonitis	Silicosis with Progressive massive fibrosis	Silicosis with progressive massive fibrosis
37 Sigamani	D1 D2	D1 D2	restrictive	same as above	same as above	Silicosis with progressive massive fibrosis	silicosis with progressive massive fibrosis

38	Rajendran	D4 D2	D4 D2	Restrictive	tuberculosis silicosis treated lymphoma histoplamosis	sarcoidosis NSIP hypersensitivity pneumonitis CVD IPF Bronchitis Infections	Silicosis	Silicosis
39	Malmrkodi	D1 D2	D1 D2 D4	not donejon ventilatory supp	Xray Chest ARDS Bacterial pneumonia Aspiration pneumonia Congestive cardiac failure Immunocompromised Pneumonia Viral pneumonia	ARDS diffuse alveolar damage Aspiration pneumonia CVD, NSIP,Hypersensitivity pneumonitis	ARDS	ARDS
40	Sekar	D1 D2	D1 D2 D4	not done	same as above	same as above	ARDS	ARDs
41	Sathyapriya	D1 D2 D3	D1 D2 D3 D7	obstructive	HRCT ABPA Cystic fibrosis William campbell syndrome	ABPA Chronic eosinophilic pneumonia Asthma Churg strauss Hypersensitivity pneumonitis	ABPA	ABPA
42	Prabha	D1 D2 D3	D1 D2 D3 D7	obstructive	same as above	same as above	ABPA	ABPA
43	Foluncool	D1 D2	D1 D2	restrictive	radiation pneumonitis lymphangitis carcinomatosis lymphocytic interstitial pneumonia pulmonary edema viral pneumonia	D1 D2 BAL cytology positive for malignant cells hence lymphangitic carcinomatosa	lymphangitic carcinomatosa	lymphangitic carcinomatosa
44	Rathinamvel	D1 D2	D1 D2 D4	restrictive	same as above	D1 D2 D4 BAL cytology positive for malignant cells,hence Lymphangitic carcinomatosa	lymphangitic carcinomatosa	Lymphangitic carcinomatosa
45	Revathy	D2 D3	D1 D2	mixed	Chronic aspiration pneumonitis tuberculosis endobronchial spread Aspiration bronchiolitis other bronchiolitis	aspiration pneumonia CVD IPF Bronchitis Infections	Aspiration bronchiolitis	Aspiration bronchiolitis
46	Selvarani	D1 D2	D1 D2	restrictive	IPF Chronic hypersensitivity pneumonitis CVD Drug induced ILD Sarcoidosis Silicosis	IPF CVD Hypersensitivity pneumonitis sarcoidosIs	IPF	IPF
47	Ranganathan	D1 D2	D1 D2 D4	mixed	Chronic hypersensitivity pneumonitis Sarcoidosis Silicosis IPF NSIP	sarcoidosis hypersensitivity pneumonitis NSIP IPF,CVD Bronchitis Infections	Chronic hypersensitivity pneumonitis	Chronic hypersensitivity pneumonitis
48	Sarala	D1 D2	D1 D2	restrictive	old ggo mild honeycombing basal pulmonary hemorrhage,edema viral/gcp pneumonia hypersensitivity pneumonitis Chronic eosinophilic pneumonia NSIP Rheumatoid lung	IPF,CVD,Bronchitis hypersensitivity pneumonitis	rheumatoid ILD(CVD)	Rheumatoid ILD(CVD)
49	Rajamani	D1 D2	D1 D2 D4	mixed	DD fibrosis sarcoidosis silicosis Hypersensitivity pneumonitis scleroderma asbestosis	Hypersensitivity pneumonitis NSIP Sarcoidosis Bronchitis	Chronic hypersensitivity Pneumonitis	Chronic hypersensitivity pneumonitis
50	Kutty	D1 D2	D1D2 D4	mixed	same as above	same as above	chronic hypersensitivity pneumfonitis	chronic hypersensitivity pneumonitis